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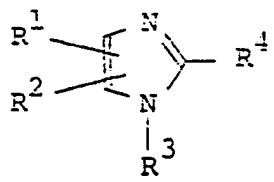
(54) Imidazole compounds, processes for the preparation thereof and pharmaceutical composition comprising the same.

(57) A compound of the formula :



wherein
R^1 is pyridyl,
R^2 is hydrogen, lower alkyl or hydroxy (lower) alkyl,
R^3 is hydrogen, hydroxy or lower alkyl, and R^4 is aryl optionally substituted with substituent(s) selected from the group consisting of low r alkylthio, lower alkylsulfinyl, low r alkylsulfonyl, nitro, amino,

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substituted amino, hydroxy, lower alkoxy, lower alkynyloxy, substituted or unsubstituted ar(lower)alkoxy, halogen, halo(lower)alkyl, carboxy and esterified carboxy,

and a pharmaceutically acceptable salt thereof, processes for the preparation thereof and pharmaceutical composition comprising the same

IMIDAZOLE COMPOUNDS, PROCESSES FOR THE PREPARATION THEREOF AND PHARMACEUTICAL COMPOSITION COMPRISING THE SAME

This invention relates to new imidazole compounds and pharmaceutically acceptable salts thereof.

More particularly, this invention relates to new imidazole compounds and pharmaceutically acceptable salts thereof which have pharmacological activities, processes for the preparation thereof, a pharmaceutical composition comprising the same and method for the therapeutic treatment thereby.

One object of this invention is to provide the new and useful imidazole compounds and pharmaceutically acceptable salts thereof which possess cardiotonic activity and the capability of reducing heart rate; anti-platelet activity; and/or anti-inflammatory activity.

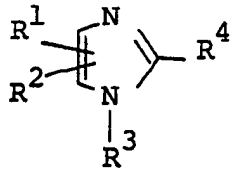
Another object of this invention is to provide processes for the preparation of the imidazole compounds and salts thereof.

A further object of this invention is to provide a pharmaceutical composition comprising, as active ingredients, said imidazole compounds or pharmaceutically acceptable salts thereof.

Still further object of this invention is to provide a method for therapeutic treatment of heart disease, thrombosis and inflammation of human beings or animals by administering said imidazole compounds or pharmaceutically acceptable salts thereof.

Some imidazole compounds having substituted or unsubstituted phenyl at 2-position of the imidazole ring have been known as described in U.S. Patent Nos. 3,707,475, 4,440,774, etc..

The object imidazole compounds of this invention are novel and can be represented by the following general formula [I] :



[I]

wherein

R^1 is pyridyl,

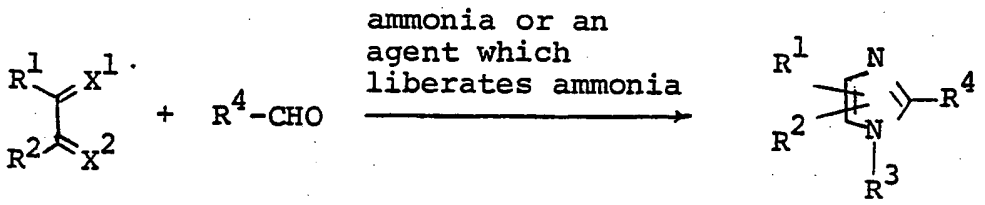
R^2 is hydrogen, lower alkyl or hydroxy(lower)alkyl,

R^3 is hydrogen, hydroxy or lower alkyl, and

R^4 is aryl optionally substituted with substituent(s) selected from the group consisting of lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, nitro, amino, substituted amino, hydroxy, lower alkoxy, lower alkynyloxy, substituted or unsubstituted ar(lower)alkoxy, halogen, halo(lower)alkyl, carboxy and esterified carboxy.

The object compound [I] or its salt can be prepared by processes as illustrated in the following reaction schemes.

Process 1

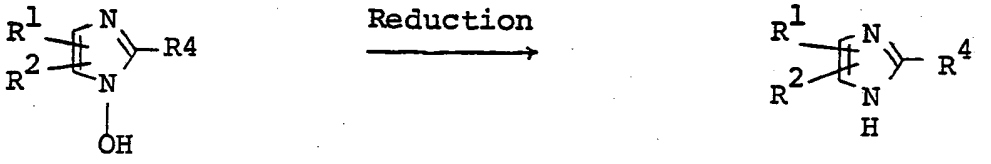


[II] or its salt

[III] or its salt

[I] or its salt

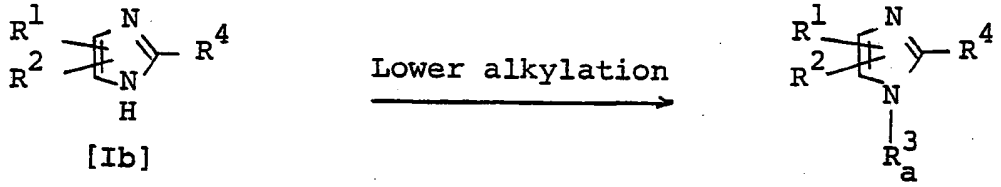
Process 2



[Ia] or its salt

[Ib] or its salt

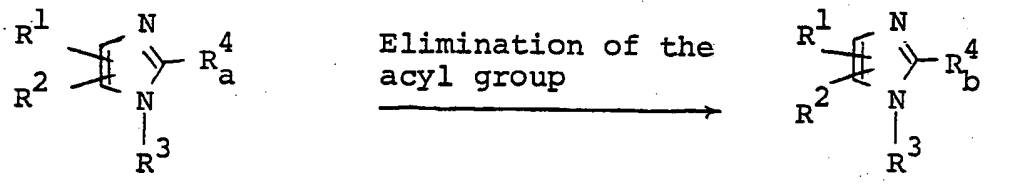
Process 3



[Ib] or its salt

[Ic] or its salt

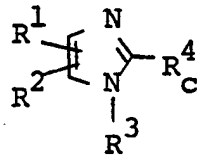
Process 4



[Id] or its salt

[Ie] or its salt

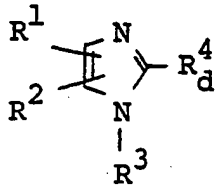
Process 5



[If]

or its salt

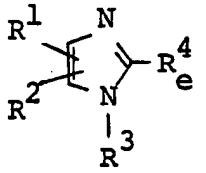
Acylation



[Ig]

or its salt

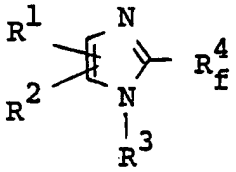
Process 6



[Ih]

or its salt

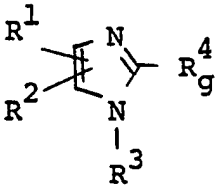
Oxidation



[Ii]

or its salt

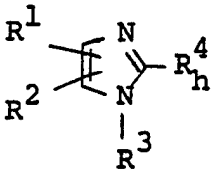
Process 7



[Ij]

or its salt

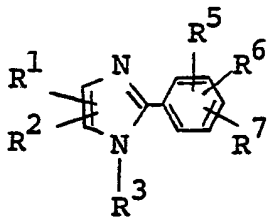
Reduction



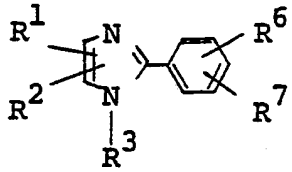
[Ik]

or its salt

Process 8



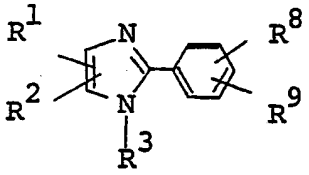
Reduction



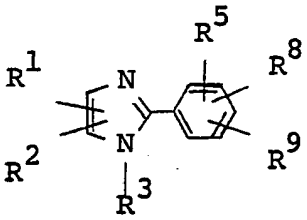
[Iℓ] [Im]

or its salt or its salt

Process 9



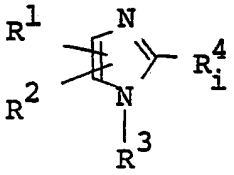
Halogenation



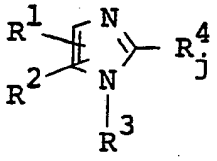
[Iη] [Io]

or its salt or its salt

Process 10



Reduction



[Ip] [Iq]

or its salt or its salt

wherein

R_a^3 is lower alkyl,

R_a^4 is aryl substituted with acylamino and lower alkoxy, with acylamino, lower alkoxy and halog n, or with N-acyl-N-low r alkylamino, lower alkoxy and halogen,

R_b^4 is aryl substituted with amino and lower alkoxy, with amino, lower alkoxy and halogen, or with lower alkylamino, lower alkoxy and halogen,

R_c^4 is aryl substituted with amino, with amino and lower alkyl, with amino and lower alkoxy, with

amino and halogen, with amino, lower alkoxy and nitro, or with amino, lower alkoxy and halogen,

R^{4}_{d} is aryl substituted with acylamino, with acylamino and lower alkyl, with acylamino and lower alkoxy, with acylamino and halogen, with acylamino, lower alkoxy and nitro, or with acylamino, lower alkoxy and halogen,

R^{4}_{e} is aryl substituted with lower alkylthio and lower alkoxy,

R^{4}_{f} is aryl substituted with lower alkylsulfinyl and lower alkoxy, or with lower alkylsulfonyl and lower alkoxy,

R^{4}_{g} is aryl substituted with nitro, with nitro and lower alkoxy, or with nitro, lower alkoxy and halogen,

R^{4}_{h} is aryl substituted with amino, with amino and lower alkoxy, or with amino, lower alkoxy and halogen,

R^{4}_{i} is aryl substituted with ar(lower)alkoxy and lower alkoxy,

R^{4}_{j} is aryl substituted with hydroxy and lower alkoxy,

R^5 is halogen,

R^6 and R^7 are each lower alkoxy or substituted amino,

R^8 and R^9 are each lower alkoxy,

one of X^1 and X^2 is O and the other is a group of the formula : $=N-R^3$, in which R^3 is as defined above, and

R^1, R^2, R^3 and R^4 are each as defined above.

In the above and subsequent description of the present specification, suitable examples of the various definitions to be included within the scope of the invention are explained in detail in the following.

The term "lower" is intended to mean a group having 1 to 6 carbon atom(s), unless otherwise provided.

Suitable "lower alkyl" and lower alkyl moiety in the term "hydroxy(lower)alkyl" may be a straight or branched one such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl or the like, in which the preferable one is C_1-C_4 alkyl and the most preferable one is methyl or ethyl.

Suitable "aryl" may be phenyl, naphthyl, lower alkyl substituted phenyl [e.g. tolyl, mesityl, cumenyl, etc.] or the like, in which the preferable one is phenyl or tolyl.

The aryl group for R^4 may be substituted with lower alkylthio [e.g. methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio, tert-butylthio, pentylthio, hexylthio, etc.], lower alkylsulfinyl [e.g. methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl, butylsulfinyl, isobutylsulfinyl, tert-butylsulfinyl, pentylsulfinyl, hexylsulfinyl, etc.], lower alkylsulfonyl [e.g. methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, isobutylsulfonyl, tert-butylsulfonyl, pentylsulfonyl, hexylsulfonyl, etc.], nitro, amino, substituted amino such as mono-or di(lower)alkylamino [e.g. methylamino, ethylamino, propylamino, dimethylamino, diethylamino, methylethylamino, etc.], acylamino [e.g. lower alkanoylamino (e.g. formylamino, acetylamino, propionylamino, hexanoylamino, pivaloylamino, etc.), substituted or unsubstituted aroylamino (e.g. benzoylamino, 3-nitrobenzoylamino, 4-chlorobenzoylamino, etc.), lower alkoxycarbonylamino (e.g. methoxycarbonylamino, ethoxycarbonylamino, tert-butoxycarbonylamino, tert-pentyloxycarbonylamino, hexyloxycarbonylamino, etc.), ar(lower)alkoxycarbonylamino (e.g. benzyloxycarbonylamino, etc.), lower alkanesulfonylamino (e.g. mesylamino, ethanesulfonylamino, etc.), arenesulfonylamino (e.g. benzenesulfonylamino, tosylamino, etc.), ureido, thioureido, lower alkylureido (e.g. methylureido, ethylureido, propylureido, isopropylureido, etc.), lower alkylthioureido (e.g. methylthioureido, ethylthioureido,propylthioureido, isopropylthioureido,etc.), aroylthioureido(e.g. benzoylthioureido, etc.),etc.], N-acyl-N-lower alkylamino [e.g. N-lower alkanoyl-N-lower alkylamino (e.g. N-acetyl-N-methylamino, etc.), etc.] or the like, hydroxy, lower alkoxy [e.g. methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, tert-butoxy, pentyloxy, hexyloxy, etc.], lower alkynyloxy [e.g. ethynyloxy, propynyloxy, butynyloxy, etc.], substituted or unsubstituted ar(lower)alkoxy [e.g. benzyloxy, phenethyloxy, benzhydryloxy, 4-chlorobenzyloxy, etc.], halogen [e.g. fluorine, chlorine, bromine and iodine], halo(lower)alkyl [e.g. chloromethyl, chloroethyl, trifluoromethyl, etc.], carboxy or esterified carboxy [e.g. lower alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, tert-pentyloxycarbonyl, hexyloxycarbonyl, etc.), etc.], wherein the number of the substituent(s) is 1 to 3 and plural substituents may be the same or different.

Suitable substituents of aryl for R^{4}_{a} to R^{4}_{j} can be referred to the ones as exemplified for the substituents of aryl for R^4.

Suitable "halogen" for R^5, "lower alkoxy" and "substituted amino" for R^6 and R^7 and "lower alkoxy" for R^8 and R^9 can be referred to the ones as exemplified for the substituents of aryl for R^4.

Suitable pharmaceutically acceptable salts of the object compound [I] are conventional non-toxic salts and include an organic acid addition salt [e.g. formate, acetate, trifluoroacetate, maleate, tartrate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.], an inorganic acid addition salt [e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.], a salt with an acidic amino aicd [e.g. aspartic acid salt, glutamic acid salt, etc.], and the like.

With respect to the salt of th compounds [Ia] to [Iq] in the Processes 1 to 10, it is to be noted that these compounds are included within the scope of the compound [I], and accordingly the suitable examples of the salts of these compounds are to be referred to those as exemplified for the object compound [I].

The processes for preparing the object compounds [I] of the present invention are explained in detail in the following.

Process 1

The object compound [I] or its salt can be prepared by reacting a compound [II] or its salt with a compound [III] or its salt in the presence of ammonia or an agent which liberates ammonia.

Suitable salts of the compound [II] may be the same as those exemplified for the compound [I] and further a base salt such as an alkali metal salt [e.g. lithium salt, sodium salt, potassium salt, etc.] or the like.

Suitable salts of the compound [III] may be the same as those exemplified for the compound [I].

This reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, propanol, etc.], acetic acid, dioxane, tetrahydrofuran, methylene chloride, chloroform, acetonitrile, N,N-dimethylformamide, dimethyl sulfoxide or any other organic solvent which does not adversely influence the reaction, or a mixture thereof.

Suitable agents which liberates ammonia may be ammonium lower alkanoate [e.g. ammonium formate, ammonium acetate, ammonium propionate, ammonium butyrate, etc.], ammonium carbonate, ammonium hydrogencarbonate, ammonium carbamate or the like.

The reaction temperature is not critical, and the reaction is usually carried out under cooling, at ambient temperature or under warming or heating.

Process 2

The object compound [Ib] or its salt can be prepared by reducing a compound [Ia] or its salt.

The reduction can be carried out in a conventional manner, namely, chemical reduction or catalytic reduction.

Suitable reducing agents to be used in chemical reduction are a metal hydride compound such as aluminum hydride compound [e.g. lithium aluminum hydride, sodium aluminum hydride, aluminum hydride, lithium trimethoxyaluminum hydride, lithium tri-t-butoxyaluminum hydride, etc.], borohydride compound [e.g. sodium borohydride, lithium borohydride, sodium cyanoborohydride, tetramethylammonium borohydride, etc.], borane, diborane, aluminum halide [e.g. aluminum chloride, etc.], phosphorus trihalide [e.g. phosphorus trichloride, phosphorus tribromide, etc.], tri(lower)alkyl phosphite [e.g. triethyl phosphite, etc.], ferrous oxalate, a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.] or the like.

Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalyst [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel,etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Ullman copper, etc.] or the like.

The reaction of this process is usually carried out in a solvent such as water, alcohol [e.g. methanol, ethanol, propanol, etc.], acetic acid, diethyl ether, dioxane, tetrahydrofuran, methylene chloride, chloroform, N,N-dimethylformamide, dimethylsulfoxide, or any other organic solv nt which does not adversely influence the reaction, or a mixtur thereof.

The reaction is preferably carried out under somewhat milder conditions such as under cooling to warming.

In this reaction condition, hydroxy(low r)alkyl for R^2 may be obtained from the corresponding lower alkyl, and thus obtained product is also included within the scope of this process.

Process 3

The object compound [Ic] or its salt can be prepared by subjecting a compound [Ib] or its salt to lower alkylation reaction.

Suitable lower alkylating agents to be used in this reaction may be lower alkyl halide [e.g. methyl iodide, ethyl iodide, propyl iodide, butyl iodide, butyl chloride, pentyl chloride, etc.], 2-lower alkylthio-2-imidazoline [e.g. 2-methylthio-2-imidazoline, etc.], lower alkyl sulfonate [e.g. methyl benzenesulfonate, ethyl mesylate, etc.], di(lower)alkyl sulfate [e.g. dimethyl sulfate, diethyl sulfate, etc.] or the like.

This reaction is usually carried out in the presence of a base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydride or hydroxide thereof, alkali metal alkoxide [e.g. sodium methoxide, sodium ethoxide, potassium tert-butoxide, etc.], trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]-octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, or the like.

This reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, propanol, etc.], tetrahydrofuran, dioxane, ethyl acetate, methylene chloride, N,N-dimethylformamide, dimethyl sulfoxide, diethyl ether or any other organic solvent which does not adversely influence the reaction. And in case that the above-mentioned lower alkylating agent is in liquid, it can be also used as a solvent.

The reaction temperature is not critical, and the reaction is usually carried out under cooling, at ambient temperature or under warming or heating.

Process 4

The object compound [Ie] or its salt can be prepared by subjecting a compound [Id] or its salt to elimination reaction of the acyl group.

This reaction is carried out in accordance with a conventional method such as hydrolysis, reduction or the like.

The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid. Suitable base may be an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, alkali metal alkanoate [e.g. sodium acetate, etc.], or the like. Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.] and an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, etc.]. The elimination using Lewis acid such as trihaloacetic acid [e.g. trichloroacetic acid, trifluoroacetic acid, etc.] or the like is preferably carried out in the presence of cation trapping agents [e.g. anisole, phenol, etc.].

The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], methylene chloride, tetrahydrofuran, a mixture thereof of any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent. The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

The reduction method applicable for the elimination reaction may include chemical reduction and catalytic reduction.

Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.].

Suitable catalysts to be used in catalytic reduction can be referred to the ones as exemplified in Process 2.

The reduction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, methanol, ethanol, propanol, N,N-dimethylformamide, or a mixture thereof. Additionally, in case that the above-mentioned acids to be used in chemical reduction are in liquid, they can also b used as a solvent. Further, a suitable solvent to be used in catalytic r duction may be the above-mentioned solvent, and other conventional solvent such as diethyl ether, dioxane, tetrahydrofuran, etc., or a mixture thereof. The reaction t mperature is not critical and the reaction is usually carried out under cooling to warming.

Process 5

The object compound [Ig] or its salt can be prepared by reacting a compound [If] or its salt with an acylating agent.

Suitable acylating agents are the corresponding acid compounds, which are represented by the formula : R^{10}-OH wherein R^{10} is acyl, and its reactive derivative, and the corresponding isocyanate or isothiocyanate compounds.

As suitable said reactive derivatives, there may be mentioned acid halides, acid anhydrides, active amides and active esters. Suitable examples are acid halides such as acid chloride and acid bromide, mixed acid anhydrides with various acids [e.g. substituted phosphoric acid such as dialkyl phosphoric acid, sulfuric acid, aliphatic carboxylic acid, aromatic carboxylic acid, etc.], symmetric acid anhydrides, active amides with various imidazoles, and active esters such as cyanomethyl ester, methoxymethyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester, pentachlorophenyl ester, phenylazophenyl ester, carboxymethyl-thio ester and N-hydroxysuccinimide ester. The kind of such reactive derivatives can be selected depending on the kind of acyl group to be introduced.

The reaction is usually carried out in a conventional solvent, such as alcohol [e.g. methanol, ethanol, etc.], methylene chloride, chloroform, benzene, toluene, pyridine, diethyl ether, dioxane, tetrahydrofuran, acetone, acetonitrile, ethyl acetate, acetic acid, N,N-dimethylformamide or any other organic solvent which does not adversely affect the reaction. In case that the acylating agent is liquid, it can also be used as a solvent. In case that the carboxylic acid compounds are used as acylating agent in the free acid form or salt form, it is preferable to carry out the reaction in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide or the like.

The reaction temperature is not critical and the reaction can be carried out under cooling, at ambient temperature, or under heating.

This reaction is preferably carried out in the presence of an inorganic base, for example an alkali metal hydroxide such as sodium hydroxide or potassium hydroxide, or an alkali metal carbonate or hydrogen carbonate such as sodium carbonate, potassium carbonate, sodium hydrogen carbonate or potassium hydrogen carbonate, or in the presence of an organic base, for example a tertiary amine such as triethylamine, pyridine or N,N-dimethylaniline.

Process 6 :

The compound [Ii] or its salt can be prepared by oxidizing a compound [Ih] or its salt.

The present oxidation reaction can be carried out by a conventional method which is applied for the transformation of -S-into -SO-or -SO_2-, for example by using an oxidizing agent such as m-chloroperbenzoic acid, perbenzoic acid, peracetic acid, ozone, hydrogen peroxide, periodic acid, potassium permanganate or the like.

The present reaction is usually carried out in a solvent such as water, acetone, dioxane, acetonitrile, acetic acid, chloroform, ethylene chloride, ethyl acetate or any other solvents which do not adversely affect the reaction.

The reaction temperature is not critical, and the reaction is preferably carried out under cooling or at ambient temperature.

Process 7

The object compound [Ik] or its salt can be prepared by reducing a compound [Ij] or its salt.

The reduction can be carried out in a conventional manner, namely, chemical reduction or catalytic reduction.

Suitable reducing agents to be used in chemical reduction may be a combination of metal [e.g. tin, zinc, iron, etc.] and ammonium chloride or a. base [e.g. ammonia, sodium hydroxide, etc.], a combination of the above-mentioned metal or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.], alkali metal borohydride [e.g. lithium borohydride, sodium borohydride, potassium borohydride etc.], alkali metal cyanoborohydrid [e.g. sodium cyanoborohydride, etc.] or alkali metal aluminum hydride [e.g. lithium aluminum hydride, etc.] or the like.

Suitable catalysts to be used in catalytic reduction can be referred to the ones as exemplified in Process 2.

The reaction of this process is usually carried out in a solvent such as wat r, alcohol [e.g. methanol, ethanol, propanol, etc.], acetic acid diethyl ether, dioxane, tetrahydrofuran, etc. or a mixture thereof.

The reaction is usually carried out under cooling to warming or heating.

Process 8

The object compound [Im] or its salt can be prepared by reducing a compound [Il] or its salt.

This reaction can be carried out in substantially the same manner as that of Process 7, and therefore the reaction mode and reaction conditions of this reaction can be referred to those as explained in Process 7.

Process 9

The object compound [Io] or its salt can be prepared by halogenating a compound [In] or its salt.

The halogenation is carried out in the presence of a halogenating agent.

Suitable halogenating agents of this reaction may be halogen [e.g. chlorine, bromine, iodine, etc.], sulfuryl halide [e.g. sulfuryl chloride, sulfuryl bromide, etc.], N-halosuccinimide [e.g. N-chlorosuccinimide, N-bromosuccinimide, etc.], pyridinium hydrohalide perhalide [e.g. pyridinium hydrobromide perbromide, pyridinium hydrochloride perchloride, etc.], quarternary ammonium perhalide [e.g. phenyltrimethylammonium perbromide, etc.], ω-trihaloacetophenone[e.g. ω-tribromoacetophenone, etc.], selenium oxychloride and the like. These halogenating agents may be selected according to the kind of the starting compound [In] to be used.

This reaction is usually carried out in a conventional solvent such as chloroform, methylene chloride, carbon tetrachloride, N,N-dimethylformamide, acetic acid, a mixture of hydrogen halide [e.g. hydrogen bromide, hydrogen chloride, etc.] and acetic acid or the like.

The reaction temperature is not critical, and the reaction is usually carried out at ambient temperature or under warming or heating.

Process 10

The object compound [Iq] or its salt can be preparred by reducing a compound [Ip] or its salt.

This reaction can be carried out by a catalytic reduction method.

This catalytic reduction can be carried out in substantially the same manner as that of Process 7, and therefore the reaction mode and reaction conditions of this reaction can be referred to those as explained in Process 7.

The compounds obtained by the above processes are isolated and purified by a conventional method such as pulverization, recrystallization, column chromatography, reprecipitation or the like.

The new imidazole compounds [I] and pharmaceutically acceptable salts thereof possess cardiotonic activity and the capability of reducing heart rate; anti-platelet activity; and/or anti-inflammatory activity, and are useful for a therapeutic treatment of heart diseases such as cardiac insufficiency, thrombosis, and inflammation.

For therapeutic purpose, the compound [I] and a pharmaceutically acceptable salt thereof of the present invention can be used in a form of pharmaceutical preparation containing one of said compounds, as an active ingredient, in admixture with a pharmaceutically acceptable carrier such as an organic or inorganic solid or liquid excipient suitable for oral, parenteral or external administration. The pharmaceutical preparations may be capsules, tablets, dragees, granules, solution, suspension, emulsion, or the like. If desired, there may be included in these preparations, auxiliary substances, stabilizing agents, wetting or emulsifying agents, buffers and other commonly used additives.

While the dosage of the compound [I] will vary depending upon the age and condition of the patient, an average single dose of about 0.1 mg, 1 mg, 10 mg, 50 mg, 100 mg, 250 mg, 500 mg and 1000 mg of the compound [I] may b effective for tr ating the above-mentioned diseases. In g neral, amounts between 0.1 mg/body and about 1,000 mg/body may be administered per day.

In order to illustrate the usefulness of the object compound [I], the pharmacological test data of some representative compounds of the compound [I] are shown in the following.

Test Compounds 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole
(hereinafter referred to as Compound a)

2-(2,4-Dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole
(hereinafter referred to as Compound b)

2-(2-Methoxy-4-methylthiophenyl)-5-methyl-4-(3-pyridyl)imidazole
(hereinafter referred to as Compound c)

2-(3,4-Dimethoxyphenyl)-5-ethyl-4-(2-pyridyl)imidazole
(hereinafter referred to as Compound d)

2-(2,4-Dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole
(hereinafter referred to as Compound e)

2-(2,4-Dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole
(hereinafter referred to as Compounf f)

2-(4-Acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole
(hereinafter referred to as Compound g)

2-(2-Methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole
(hereinafter referred to as Compound h)

2-(2-Fluorophenyl)-4-methyl-5-(3-pyridyl)imidazole
(hereinafter referred to as Compound i)

2-(2-Acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole
(hereinafter referred to as Compound j)

2-(4-Chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole
(hereinafter referred to as Compound k)

Cardiotonic activity

Test 1

Test method

Mongrel dogs of either sex were anesthetized with sodium pentobarbital, 35 mg/kg, i.p.. The animals were allowed to breathe spontaneously. The left carotid artery was isolated and a catheter (USCI, #8F) filled with heparinized saline was inserted and advanced into the left ventricle. The catheter was connected to a pressure transducer (Nihonkohden, MPU-0.5A) to measure the left ventricular pressure, from which dp/dt max was derived by analog computing. The measure the systemic blood pressure the left femoral artery was cannulated. The blood pressure pulse was used to trigger a heart rate meter. Another catheter was positioned in the vena cave through right femoral vein for injection of drugs. Systemic blood pressure, left ventricular pressure, dp/dt max and heart rate were recorded simultaneously on a polygram (Nihonkohden, RJG-4008).

Test compound was dissolved in distilled water (0.2 ml/kg) or dimethyl sulfoxide (0.04 ml/kg) and injected into the femoral vein. The parameters after dosing were compared with those during the predosing period.

Test results wer represented in terms of percentag of dp/dt max chang s (dp/dt M.C.) calculated by following formula.

$$dp/dt\ M.C.\ (\%) = \left(\frac{dp/dt\ max\ after\ dosing}{dp/dt\ max\ before\ dosing} - 1\right) \times 100$$

Test Results

Compound	Dose (mg/kg)	dp/dt M.C. (%)
a	1.0	82
b	1.0	133
c	1.0	167

Test 2

Test Method

Male Hartley strain guinea-pigs, weighing 530-600 g, were killed by bleeding and the heart was removed. An atrial strip was removed and suspended in an organ bath containing 50 ml of Tyrode's solution maintained at 30°C and aerated with a gas mixture of 95% O_2 -5% CO_2. The atrium was connected to a strain gauge under an initial tension of 0.4-0.6 g. After constant motility had been obtained the drug was added to the bath solution and the effect on contractile force and heart rate was observed for 30 min. The effect was expressed as percentage values before and after dosing.

Test Results

Compound	Concentration (g/ml)	Force (%)	Heart Rate (%)
a	1×10^{-5}	45.0	-21.2
d	1×10^{-5}	51.6	-14.1
e	1×10^{-5}	58.0	-26.8
f	1×10^{-5}	61.1	-30.7

Anti-platelet activity

Test 3

Test Method

Male Sprague-Dawley rats weighing about 250 g were used after overnight fasting. One hour after oral administration of test compound or vehicle of test compound (control), blood was collected into a tube containing 0.1 vol. of 3.8% sodium citrate. To the 0.45 ml of blood, 0.05 ml of collagen (final concentration 5.0 μg/ml) was added and then incubated for 5 min. at 37°C. under shaking. The reaction was terminated by addition of 1 ml of 10 mM phosphate buffered saline (pH 7.4) containing 11.5 mM EDTA and 1% formalin. The reaction mixture was centrifuged at 70xg for 5 min. and platelet count of upper phase was measured by Technicon Auto Analizer. Platelet aggregation was calculated according to the following formula :

$$\text{Platelet aggregation (\%)} = \frac{A - B}{A} \times 100$$

A : Platelet count after addition of vehicle of collagen

B : Platelet count after addition of collagen

Inhibition of the test compound was calculated according to the following formula :

$$\text{Inhibition (\%)} = \frac{C - D}{C} \times 100$$

C : Platelet aggregation (%) of control

D : Platelet aggregation (%) of Test compound

Test Results

Compound	Dose (mg/kg)	Inhibition (%)
g	32	87.6
i	32	100
j	32	91.3

Test 4

Test Method

The blood was collected from the carotid artery of rabbits into plastic vessels containing 0.1 volume of 3.8% sodium citrate. Platelet rich plasma (PRP) was prepared by centrifugation at 150 g for 15 minutes. Platelet aggregation was investigated by using the turbidimetric method with an aggregometer (NKK HEMATRACER 1). To the 225 μl of PRP, 25 μl of test compound solution was added, and then stirred at 1000 rpm for 2 minutes at 37°C. To the solution 5 μl of 9, 11-azo PGH_2 (final 1.0 μM) was added as an aggregating inducer.

Test Results

Compound	IC_{50} (g/ml)
i	1.1×10^{-7}
j	3.9×10^{-7}
k	1.6×10^{-7}

Anti-inflammatory activity

Test 5

Test Method

Male Sprague-Dawley rats weighing about 180 g were used in groups of five. Paw edema was induced by subplantar injection of 1% carrageenin (0.1 ml/rat) into the right hind paw in carrageenin foot edema. The test compound was suspended in methylcellulose and administered orally 60 minutes before halogogen. Paw volume was measured with plethysmometer (Ugo Basil Co., Ltd.) by water displacement immersing the paw to the lateral malleolus. The difference of paw volume before and 3 hours after the phlogogen was designated as edema volume.

The data was analyzed statistically by student's t-test.

Test Results

Compound	Dose (mg/kg)	Inhibition (%)
h	32	62.7
k	32	72.3

The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

Preparation 1

To a solution of isoamyl nitrite (2.6 ml) and sodium methoxide (28% in methanol, 3.4 ml) in methanol (40 ml) was added dropwise a solution of 4-propionylpyridine (2.0 g) in methanol (10 ml) under ice-cooling. The reaction mixture was stirred at ambient temperature for 3 hours, and then neutralized with 1N hydrochloric acid. After evaporation to remove methanol, the organic layer was extracted with ethyl acetate. The extract was washed with brine, dried over sodium sulfate, evaporated and triturated with diisopropyl ether to give 4-(2-hydroxyiminopropionyl)pyridine (0.95 g).

mp : 150-151°C

IR (Nujol) : 1670, 1605 cm^{-1}

NMR ($CDCl_3$, δ) : 2.15 (3H, s), 7.65 and 8.60 (4H, AB type, J = 7Hz)

The following compounds (Preparations 2 to 4) were obtained according to a similar manner to that of Preparation 1.

Preparation 2

4-(2-Hydroxyiminobutyryl)pyridine
mp : 146-149°C
IR (Nujol) : 3250, 1680, 1590 cm^{-1}

Preparation 3

1-Hydroxyimino-1-(3-pyridyl)-2-butanone
mp : 172-174°C
IR (Nujol) : 1690, 1600, 1585 cm^{-1}
NMR (DMSO-d_6, δ) : 1.10 (3H, t, J=7Hz), 2.98 (2H, q, J=7Hz), 7.45 (1H, dd, J=8Hz, J=8Hz), 7.70 (1H, ddd, J=8Hz, J=2Hz, J=2Hz), 8.45-8.70 (2H, m)

Preparation 4

2-(2-Hydroxyiminobutyryl)pyridine
mp : 134-135°C
IR (Nujol) : 1670, 1580, 1490 cm^{-1}
NMR ($CDCl_3$, δ) : 1.16 (3H, t, J=7Hz), 2.78 (2H, q, J=7Hz), 7.2-7.5 (1H, m), 7.7-8.1 (1H, m), 7.90 (1H, d, J=2Hz), 8.63 (1H, dd, J=5.5Hz, 2Hz)

Example 1

To a suspension of 4-(2-hydroxyiminopropionyl)pyridine (2.0 g) in a mixture of dioxane (40 ml) and ethanol were added conc. ammonia water (58 ml) and 2,4-dimethoxybenzaldehyde (2.02 g), and the mixture was stirred at ambient temperature for 1 week. After evaporation, the mixture was triturated with chloroform to give 1-hydroxy-2-(2,4-dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole (3.01 g).
mp : 240-241°C
IR (Nujol) : 1605 cm^{-1}
NMR (DMSO-d_6, δ) : 2.38 (3H, s), 3.77 (3H, s), 3.83 (3H, s), 6.5-6.9 (2H, m), 7.31 (1H, d, J=8Hz), 7.67 (2H, d, J=6Hz), 8.55 (2H, d, J=6Hz)

Example 2

To a suspension of 1-hydroxyimino-1-(3-pyridyl)acetone (1.5 g) in a mixture of dioxane (30 ml) and ethanol (8 ml) were added conc. ammonia water (40 ml) and 2-methoxybenzaldehyde (1.24 g), and the mixture was stirred at ambient temperature for 8 days. After evaporation, the mixture was triturated with chloroform to give 1-hydroxy-2-(2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.65 g).
mp : 105-120°C
IR (Nujol) : 1605 cm^{-1}
NMR (DMSO-d_6, δ) : 2.22 (3H, s), 3.73 (3H, s), 6.7-7.6 (5H, m), 7.92 (1H, ddd, J=2Hz, 2Hz, 8Hz), 8.47 (1H, dd, J=2Hz, 5Hz), 8.72 (1H, d, J=2Hz)

Example 3

To a suspension of 1-hydroxyimino-1-(3-pyridyl)acetone (1.64 g) in a mixture of dioxane (30 ml), ethanol (10 ml), and water (5 ml) were added 3,4-dimethoxybenzaldehyde (1.66 g) and conc. ammonia water (0.69 ml). The solution was stirred at 60°C for 2 hours. Additional ammonia water (0.7 ml) was added thereto, and the solution was stirred at 45 to 50°C for 1 day. The mixture was evaporated, and the residue was dissolved in chloroform, and subjected to column chromatography on silicagel eluting with a mixture of chloroform and methanol. The fractions were collected and evaporated, and the residue was triturated with diisopropyl ether to give 1-hydroxy-2-(3,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.20 g).

mp : 131-135°C

IR (Nujol) : 1505, 1260, 1230 cm^{-1}

NMR (DMSO-d_6, δ) : 2.26 (3H, s), 3.80 (3H, s), 3.83 (3H, s), 7.04 (1H, d, J = 9Hz), 7.3-8.1 (4H, m), 8.56 (1H, dd, J = 2Hz, 5Hz), 8.75 (1H, d, J = 2Hz)

Example 4

To a suspension of 1-hydroxyimino-1-(3-pyridyl)acetone (3.3 g) in a mixture of dioxane (80 ml), ethanol (20 ml) and conc. ammonia water (40 ml) was added 4-acetamido-5-chloro-2-methoxybenzaldehyde (4.54 g) and the resultant mixture was stirred at ambient temperature for 3 days. The reaction mixture was evaporated in vacuo and the residue was dissolved in a mixture of ethyl acetate and 5% hydrochloric acid. The separated aqueous layer was adjusted to pH8.0 with 20% potassium carbonate under stirring and the precipitate was collected by filtration and dried to give 1-hydroxy-2-(4-acetamido-5-chloro-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (3.1 g).

mp : 178-180°C (dec.)

IR (Nujol) : 3450, 3150, 1660, 1600, 1570, 1530, 1505 cm^{-1}

NMR (D_2O - DCl, δ) : 2.35 (3H, s), 2.60 (3H, s), 4.00 (3H, s), 7.83 (1H, s), 8.07 (1H, s), 8.40 (1H, dd, J = 6Hz, 8Hz), 8.95 (1H, dd, J = 2Hz, 8Hz), 9.08 (1H, dd, J = 2Hz, 6Hz), 9.25 (1H, d, J = 2Hz)

Mass (m/e) : 372 (M^+)

Example 5

To a suspension of 1-hydroxyimino-1-(3-pyridyl)acetone (1.0 g) in a mixture of dioxane (20 ml) and ethanol (6 ml), were added 2-methoxy-4-methylbenzaldehyde (1.01 g) and conc. ammonia water (15 ml). The solution was stirred at ambient temperature for 8 days. After evaporation, the residue was dissolved in chloroform, and chromatographed on silicagel eluting with a mixture of chloroform and methanol. Th fractions were collected, evaporated, and triturated in diisopropyl ether to give 1-hydroxy-2-(2-methoxy-4-methylphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.46 g).

mp : 75-80°C

IR (Nujol) : 1615, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 2.24 (3H, s), 2.34 (3H, s), 3.75 (3H, s), 6.74 (1H, d, J = 8Hz), 6.88 (1H, s), 7.6-7.2 (2H, m), 7.87 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.43 (1H, dd, J = 5Hz, J = 2Hz), 8.65 (1H, d, J = 2Hz), 11.35 (1H, br s)

Mass : (M/Z) : 295 (M^+)

The following compounds (Examples 6 to 119) were obtained according to a similar manner to that of Example 1, 2, 3, 4 or 5.

Example 6 1-Hydroxy-2-(2,4-dimethoxyphenyl)-5-methyl-4-(2-pyridyl)imidazole

mp : 141-144°C (dec.)

IR (Nujol) : 1600, 1570, 1460, 1310, 1280 cm^{-1}

NMR ($CDCl_3$, δ) : 2.49 (3H, s), 3.73 (3H, s), 3.86 (3H, s), 6.3-6.6 (2H, m), 7.0-7.4 (1H, m), 7.6-7.8 (2H, m), 8.4-8.8 (2H, m)
Mass (m/e) : 311 (M^+)

Example 7 1-Hydroxy-2-(2,4-dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole

mp : 206-208°C (dec.)
IR (Nujol) : 1600, 1570, 1520, 1430 cm^{-1}
NMR (DMSO-d_6, δ) : 1.23 (3H, t, J=7Hz), 2.86 (2H, q, J=7Hz), 3.73 (3H, s), 3.83 (3H, s), 6.58 (1H, d, J=8Hz), 6.70 (1H, s), 7.35 (1H, d, J=8Hz), 7.65 (2H, dd, J=2Hz, 5Hz), 8.55 (2H, dd, J=2Hz, 5Hz)

Example 8 1-Hydroxy-2-(3,4-dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 131-136°C
IR (Nujol) : 1610, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.80 (3H, s), 3.83 (3H, s), 7.05 (1H, d, J=9Hz), 7.6-7.9 (4H, m), 8.23 (2H, br d, J=6Hz)

Example 9 1-Hydroxy-2-(3,4-dimethoxyphenyl)-5-methyl-4-(2-pyridyl) imidazole

mp : 141-144°C (dec.)
IR (Nujol) : 3200, 1603, 1595, 1560, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.62 (3H, s), 3.78 (3H, s) , 3.81 (3H, s), 6.99 (1H, d, J=9Hz), 7.0-7.2 (1H, m), 7.5-7.7 (2H, m), 7.75 (1H, dd, J=2Hz, 8Hz), 7.96 (1H, d, J=8Hz), 8.4-8.6 (1H, m), 10.7 (1H, br s)

Example 10 1-Hydroxy-2-(3,4-dimethoxyphenyl)-5-ethyl-4-(4-pyridyl) imidazole

IR (Nujol) : 3470, 3200, 1600, 1520, 1430 cm^{-1}
NMR (DMSO-d_6, δ) : 1.18 (3H, t, J=7Hz), 2.82 (2H, q, J=7z), 3.74 (6H, s), 6.90 (1H, d, J=9Hz), 7.6-7.8 (3H, m), 7.76 (1H, s), 8.51 (2H, dd, J=6Hz, 8Hz)

Example 11 1-Hydroxy-2-(3,4-dimethoxyphenyl)-5-ethyl-4-(2-pyridyl) imidazole

mp : 92-94°C
IR (Nujol) : 1590, 1510, 1490, 1270 cm^{-1}
NMR (DMSO-D_6, δ) : 1.24 (3H, t, J=8Hz), 3.15 (2H, q, J=8Hz), 3.80 (3H, s), 3.83 (3H, s), 7.01 (1H, d, J=9Hz), 7.0-7.2 (1H, m), 7.5-7.7 (2H, m), 7.74 (1H, dd, J=2Hz, 8Hz) 7.98 (1H, d, J=8Hz), 8.48 (1H, m), 11.6 (1H, br s)
Mass (m/e) : 325 (M^+)

Example 12 1-Hydroxy-2-(3,4-dimethoxyphenyl)-4-(2-pyridyl)imidazole

mp : 71-73°C
IR (Nujol) : 1590, 1500, 1440 cm^{-1}
NMR ($CDCl_3$, δ) : 3.94 (3H, s), 3.95 (3H, s), 6.92 (1H, d, J = 9Hz), 7.0-7.4 (2H, m), 7.5-7.9 (3H, m), 7.66 (1H, s), 8.56 (1H, d, J = 5Hz)
Mass (m/e) : 296 (M - 1)

Example 13

1-Hydroxy-5-methyl-2-phenyl-4-(3-pyridyl)imidazole
mp : 75-85°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.43 (3H, s), 7.2-7.5 (4H, m), 7.8-8.1 (3H, m), 8.34 (1H, br d, J = 4Hz), 8.81 (1H, br s), 11.7 (1H, br s)

Example 14 1-Hydroxy-2-(2,5-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 115-125°C
IR (Nujol) : 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.19 (3H, s), 3.65 (6H, s), 6.8-7.2 (3H, m), 7.30 (1H, dd, J = 5Hz, 8Hz), 7.84 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.43 (1H, dd, J = 2Hz, 5Hz), 8.66 (1H, d, J = 7Hz)

Example 15 1-Hydroxy-2-(2,4-dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole

mp : 75-80°C
IR (Nujol) : 1615, 1583 cm^{-1}
NMR (DMSO-d_6, δ) : 1.17 (3H, t, J = 7Hz), 2.40-2.55 (2H, m), 3.75 (3H, s), 3.80 (3H, s), 6.57 (1H, dd, J = 8Hz, 2Hz), 6.66 (1H, s), 7.30-7.5 (1H, m), 7.67 (1H, dd, J = 8Hz, 4Hz), 7.91 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.50 (1H, dd, J = 4Hz, 2Hz), 8.67 (1H, d, J = 2Hz)

Example 16 1-Hydroxy-2-(3,4-dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole

mp : 75-80°C
IR (Nujol) : 1608, 1587, 1512 cm^{-1}
NMR (DMSO-d_6, δ) : 1.17 (3H, t, J = 7Hz), 2.40-2.65 (2H, m), 3.75 (3H, s), 3.80 (3H, s), 7.00 (1H, d, J = 8Hz), 7.32-7.75 (3H, m), 7.86 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.50 (1H, dd, J = 4Hz, 2Hz), 8.63 (1H, d, J = 2Hz)

Example 17 1-Hydroxy-2-(2,3-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 110-115°C
IR (Nujol) : 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 2.27 (3H, s), 3.78 (3H, s), 3.86 (3H, s), 7.13 (3H, s), 7.48 (1H, dd, J=8Hz, 4Hz), 7.98 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.52 (1H, dd, J=2Hz, 4Hz), 8.75 (1H, d, J=2Hz)

Example 18 1-Hydroxy-2-(3,4,5-trimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 135-138°C
IR (Nujol) : 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.24 (3H, s), 3.73 (3H, s), 3.80 (6H, s), 7.40 (2H, s), 7.48 (1H, dd, J=8Hz, 5Hz), 7.95 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.53 (1H, br d, J=5Hz), 8.73 (1H, br s)

Example 19 1-Hydroxy-2-(2,3,4-trimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 90-100°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.26 (3H, s), 3.79 (6H, s), 3.86 (3H, s), 6.87 (1H, d, J=8Hz), 7.26 (1H, d, J=8Hz), 7.44 (1H, dd, J=8Hz, 4Hz), 7.92 (1H, ddd, J=2Hz, 2Hz, 8Hz), 8.50 (1H, dd, J=2Hz, 4Hz), 8.73 (1H, d, J=2Hz)

Example 20 1-Hydroxy-2-(2-methoxy-4-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole

NMR (DMSO-d_6, δ) : 2.31 (3H, s), 3.96 (3H, s), 7.45 (1H, dd, J=8Hz, 4Hz), 7.75-8.08 (4H, m), 8.48 (1H, d, J=4Hz), 8.73 (1H, br s)

Example 21 1-Hydroxy-2-(4-chloro-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 130-135°C
IR (Nujol) : 1600, 1575 cm^{-1}
NMR (DMSO-d_6, δ) : 2.19 (3H, s), 3.70 (3H, s), 6.83 (1H, dd, J=2Hz, 8Hz), 7.03 (1H, d, J=2Hz), 7.22 (1H, d, J=8Hz), 7.31 (1H, dd, J=8Hz, 4Hz), 7.82 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.38 (1H, dd, J=2Hz, 4Hz), 8.61 (1H, d, J=2Hz)

Example 22 1-Hydroxy-2-(4-acetamido-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 170-175°C
IR (Nujol) : 1680, 1610 cm^{-1}
NMR (DMSO-d_6, δ) : 2.05 (3H, s), 2.23 (3H, s), 3.71 (3H, s), 7.6-7.0 (4H, m), 7.86 (1H, br d, J=8Hz), 8.40 (1H, dd, J=4Hz, 2Hz), 8.64 (1H, br s), 9.96 (1H, br s), 11.05 (1H, br s)

Example 23 1-Hydroxy-2-[2-methoxy-4-(methylsulfinyl)phenyl]-4-methyl-5-(3-pyridyl)imidazole

mp : 90-95°C
IR (Nujol) : 1600, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.24 (3H, s), 2.53 (3H, s), 3.81 (3H, s), 6.7-7.0 (2H, m), 7.43 (1H, dd, J = 8Hz, 4Hz), 7.62 (1H, d, J = 8Hz), 7.92 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.48 (1H, dd, J = 2Hz, 4Hz), 8.69 (1H, d, J = 2Hz)

Example 24 1-Hydroxy-2-(2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 110-120°C
IR (Nujol) : 1610 cm^{-1}
NMR (DMSO-d_6, δ) : 2.16 (3H, s), 3.70 (3H, s), 3.77 (3H, s), 6.2-6.5 (2H, m), 7.0-7.4 (1H, m), 7.91 (1H, dd, J = 2Hz, 8Hz), 7.98 (1H, d, J = 9Hz), 8.43 (1H, dd, J = 2Hz, 5Hz), 8.56 (1H, d, J = 2Hz)

Example 25 2-(2-Fluorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 76-82°C
IR (Nujol) : 1585, 1630, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.30 (3H, s), 7.2-7.85 (5H, m), 8.00 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.60 (1H, dd, J = 5Hz, 2Hz), 8.80 (1H, d, J = 2Hz)

Example 26 2-(4-Fluorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 101-102°C
NMR (DMSO-d_6, δ) : 2.23 (3H, s), 7.12-7.56 (3H, m), 7.80-8.30 (3H, m), 8.56 (1H, d, J = 5Hz), 8.74 (1H, s)

Example 27 2-(3-Chlorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 74-84°C
IR (Nujol) : 1598, 1567 cm^{-1} NMR (DMSO-d_6, δ) : 2.25 (3H, s), 7.4-7.65 (3H, m), 7.88-8.2 (3H, m), 8.60 (1H, d, J = 5Hz), 8.78 (1H, s)

Example 28 2-(2-Chlorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 105-112°C
IR (Nujol) : 1600, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.28 (3H, s), 7.3-7.7 (5H, m), 7.95 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.3-8.8 (2H, m)

Example 29 2-(4-Chlorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 108-110°C
IR (Nujol) : 1640, 1600, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.32 (3H, s), 7.4-7.75 (3H, m), 7.85-8.3 (3H, m), 8.62 (1H, dd, J = 5Hz, 2Hz), 8.78 (1H, d, J = 2Hz)

Example 30 2-(3,4-Dichlorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 139-145°C
IR (Nujol) : 1635, 1496 cm^{-1}
NMR (DMSO-d_6, δ) : 2.4 (3H, s), 7.56 (1H, dd, J = 8Hz, 5Hz), 7.78 (1H, d, J = 8Hz), 7.9-8.2 (2H, m), 8.33 (1H, d, J = 2Hz), 8.68 (1H, dd, J = 5Hz, 2Hz), 8.8 (1H, d, J = 2Hz)

Example 31 1-Hydroxy-2-(2,4-dichlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 104-108°C
IR (Nujol) : 1596, 1552 cm^{-1}
NMR (DMSO-d_6, δ) : 2.32 (3H, s), 7.42-7.89 (4H, m), 8.07 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.67 (1H, dd, J = 5Hz, 2Hz), 8.86 (1H, d, J = 2Hz)

Example 32 2-(4-Dimethylamino-2-methoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 96-98°C
IR (Nujol) : 1607, 1611, 1562 cm^{-1}
NMR (DMSO-d_6, δ) : 2.24 (3H, s), 2.96 (6H, s), 3.82 (3H, s), 6.15-6.46 (2H, m), 7.28-7.78 (2H, m), 7.98 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.52 (1H, dd, J = 5Hz, 2Hz), 8.77 (1H, d, J = 2Hz)

Example 33 1-Hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

NMR (DMSO-d_6, δ) : 2.18 (3H, s), 3.75 (3H, s), 6.86 (2H, d, J = 8Hz), 7.25-7.52 (2H, m), 7.60 (1H, s), 7.88 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.43 (1H, dd, J = 5Hz, 2Hz), 8.66 (1H, d, J = 2Hz)

Example 34 2-(5-Chloro-2-methoxyphenyl)-1-hydroxy-4-methyl5-(3-pyridyl)imidazole

mp : 81-83°C
IR (Nujol) : 1673, 1596, 1483 cm^{-1}
NMR (DMSO-d_6, δ) : 2.26 (3H, s), 3.78 (3H, s), 7.08 (1H, d, J = 8Hz), 7.25-7.52 (3H, m), 7.91 (1H, d, J = 8Hz), 8.47 (1H, d, J = 5Hz), 8.69 (1H, s)

Example 35 1-Hydroxy-4-methyl-2-(2-methoxy-5-nitrophenyl)-5-(3-pyridyl)imidazole.

mp : 151-155°C
IR (Nujol) : 1611, 1586, 1538, 1515 cm^{-1}
NMR (DMSO-d_6, δ) : 2.30 (3H, s), 3.98 (3H, s), 7.36 (1H, d, J=9Hz), 7.48 (1H, dd, J=8Hz, 5Hz), 8.01 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.34 (1H, dd, J=8Hz, 2Hz), 8.57 (1H, dd, J=5Hz, 2Hz), 8.75 (1H, d, J=2Hz)

Example 36 1-Hydroxy-4-methyl-2-(2-methoxy-3-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 106-111°C
IR (Nujol) : 1536 cm^{-1}
NMR (DMSO-d_6, δ) : 2.30 (3H, s), 3.71 (3H, s), 7.31-8.15 (4H, m), 8.42-8.67 (2H, m), 8.31 (1H, s), 11.72 (1H, br s)

Example 37 2-(5-Chloro-2,4-dimethoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 146-149°C
IR (Nujol) : 1610 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 3.86 (3H, s), 3.96 (3H, s), 6.86 (1H, s), 7.46 (1H, dd, J=8Hz, J=4Hz), 7.80 (1H, br s), 7.97 (1H, ddd, J=8Hz, J=2Hz, J=2Hz), 8.52 (1H, dd, J=4Hz, J=2Hz), 8.73 (1H,d, J=2Hz)
Mass (M/Z) : 345 (M^+)

Example 38 2-(3-Chloro-4,5-dimethoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 123-132°C
IR (Nujol) : 1598, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.20 (3H, s), 3.76 (3H, s), 3.78 (3H, s), 7.25-8.08 (4H, m), 8.45 (1H, d, J=5Hz), 8.69 (1H, s)

Example 39 2-(3-Chloro-4-hydroxy-5-methoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 190-195°C
IR (Nujol) : 1573, 1504 cm^{-1}
NMR (DMSO-d_6, δ) : 2.21 (3H, s), 3.82 (3H, s), 7.3-7.7 (3H, m), 7.88 (1H, d, J=8Hz), 8.46 (1H, s), 8.66 (1H, s)

Example 40 1-Hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 152-155°C
IR (Nujol) : 1595, 1511 cm^{-1}
NMR (DMSO-d_6, δ) : 2.21 (3H, s), 3.76 (3H, s), 6.78 (1H, d, J = 8Hz), 7.22-7.66 (3H, m), 7.87 (1H, d, J = 8Hz), 8.45 (1H, d, J = 5Hz), 8.65 (1H, s)

Example 41 1-Hydroxy-4-methyl-2-(2-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 135-145°C
IR (Nujol) : 1613, 1530 cm^{-1}
NMR (DMSO-d_6, δ) : 2.30 (3H, s), 7.52 (1H, dd, J = 8Hz, 8Hz), 7.7-8.3 (5H, m), 8.58 (1H, dd, J = 8Hz, 2Hz), 8.75 (1H, d, J = 2Hz)

Example 42 2-[4-(N-Acetyl-N-methylamino)-5-chloro-2-methoxyphenyl]-1-hydroxy-4-methyl-5-(3-pyridyl)-imidazole

mp : 222-224°C
IR (Nujol) : 1662, 1600, 1492 cm^{-1}
NMR (DMSO-d_6, δ) : 2.31 (3H, s), 2.80 (3H, s), 3.15 (3H, s), 3.59 (3H, s), 7.35-7.62 (2H, m), 7.82-8.2 (2H, m), 8.58 (1H, dd, J = 5Hz, 2Hz), 8.77 (1H, d, J = 2Hz)
Mass (M/Z) : 385 (M^+)

Example 43 1-Hydroxy-4-methyl-2-(o-tolyl)-5-(3-pyridyl)imidazole

mp : 90-95°C
IR (Nujol) : 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 2.35 (3H, s), 7.25-7.66 (5H, m), 7.95 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.56 (1H, dd, J = 5Hz, 2Hz), 8.78 (1H, d, J = 2Hz)

Example 44 1-Hydroxy-2-(2-methoxy-4-methylsulfinylphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 205-208°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 2.54 (3H, s), 3.81 (3H, s), 6.93 (1H, d, J = 8Hz), 7.0 (1H, s), 7.35 (1H, d, J = 8Hz), 7.66 (2H, d, J = 8Hz), 8.54 (2H, d, J = 8Hz)

Example 45 1-Hydroxy-2-(3-methoxy-4-methylthiophenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 252-257°C
IR (Nujol) : 1610 cm^{-1}
NMR (DMSO-d_6, δ) : 2.46 (3H, s), 2.52 (3H, s), 3.92 (3H, s), 7.26 (1H, d, J = 8Hz), 7.9-7.6 (4H, m), 8.7-8.5 (2H, m)

Example 46 2-(2,6-Dimethoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 236-239°C
IR (Nujol) : 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 3.71 (6H, s), 6.73 (2H, d, J = 8Hz), 7.6-7.2 (2H, m), 7.96 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.48 (1H, dd, J = 5Hz, J = 2Hz), 8.75 (1H, d, J = 2Hz), 11.1 (1H, br s)

Example 47 1-Hydroxy-2-(3-methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 145-150°C
IR (Nujol) : 1630, 1600, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.24 (3H, s), 2.43 (3H, s), 3.86 (3H, s), 7.22 (1H, d, J = 8Hz), 7.50 (1H, dd, J = 8Hz, J = 5Hz), 7.9-7.65 (2H, m), 7.95 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.56 (1H, dd, J = 5Hz, J = 2Hz), 8.78 (1H, d, J = 2Hz)

Example 48 2-(4-Ethoxy-2-methoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 90-95°C
IR (Nujol) : 1615, 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 1.35 (3H, t, J = 7Hz), 2.24 (3H, s), 3.78 (3H, s), 4.10 (2H, q, J = 7Hz), 6.57 (1H, dd, J = 8Hz, J = 2Hz), 6.64 (1H, d, J = 2Hz), 7.7-7.4 (2H, m), 7.98 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.51 (1H, dd, J = 4Hz, J = 2Hz), 8.76 (1H, d, J = 2Hz)

Example 49 2-(4-Benzyloxy-2-methoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 191-193°C
IR (Nujol) : 1615, 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 3.78 (3H, s), 5.17 (2H, s), 6.68 (1H, dd, J = 2Hz, J = 8Hz), 6.77 (1H, d, J = 2Hz), 7.7-7.3 (7H, m), 7.98 (1H, ddd, J = 2Hz, J = 2Hz, J = 8Hz), 8.54 (1H, dd, J = 2Hz, J = 5Hz), 8.77 (1H, d, J = 2Hz), 11.4 (1H, br s)

Example 50 1-Hydroxy-4-methyl-5-(3-pyridyl)-2-(2,4,5-trim thoxyphenyl)imidazol

mp : 80-90°C
IR (Nujol) : 1615 cm^{-1}

NMR (DMSO-d_6, δ) : 2.25 (3H, s), 3.64 (3H, s), 3.79 (3H, s), 3.84 (3H, s), 6.78 (1H, s), 7.50 (1H, br s), 7.46 (1H, dd, J = 4Hz, J = 8Hz), 7.99 (1H, ddd, J = 2Hz, J = 2Hz, J = 8Hz), 8.53 (1H, dd, J = 2Hz, J = 4Hz), 8.77 (1H, d, J = 2Hz), 11.5 (1H, br s)
Mass (M/Z) : 341 (M^+)

Example 51 1-Hydroxy-4-methyl-5-(3-pyridyl)-2-(2,4,6-trimethoxyphenyl)imidazole

mp : 197-199°C
IR (Nujol) : 1615, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.22 (3H, s), 3.66 (6H, s), 3.82 (3H, s), 6.29 (2H, s), 7.45 (1H, dd, J = 8Hz, J = 5Hz), 7.97 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.50 (1H, dd, J = 5Hz, J = 2Hz), 8.76 (1H, d, J = 2Hz), 11.0 (1H, br s)

Example 52 1-Hydroxy-2-(4-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 95-100°C
IR (Nujol) : 1610 cm^{-1}
NMR ($CDCl_3$, δ) : 1.93 (3H, s), 3.71 (3H, s), 6.68 (2H, d, J = 9Hz), 7.18 (1H, dd, J = 5Hz, J = 8Hz), 7.5-8.0 (4H, m), 8.33 (1H, dd, J = 5Hz, J = 2Hz), 8.45 (1H, d, J = 2Hz)

Example 53 2-(5-Chloro-2-methoxy-4-methylphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole

mp : 130-135°C
IR (Nujol) : 1630, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 2.36 (3H, s), 3.79 (3H, s), 7.09 (1H, s), 7.40 (1H, br s), 7.41 (1H, dd, J = 8Hz, J = 5Hz), 7.93 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.45 (1H, dd, J = 5Hz, J = 2Hz), 8.69 (1H, d, J = 2Hz), 11.40 (1H, br s)

Example 542-(3,4-Dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 246-248°C
IR (Nujol) : 1600, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.82 (3H, s), 3.85 (3H, s), 7.04 (1H, d, J = 9Hz), 7.2-7.7 (3H, m), 8.10 (1H, br d, J = 8Hz), 8.45 (1H, br d, J = 6Hz), 8.92 (1H, br s)

Example 55 2-(3,4-Dimethoxyphenyl)-5-methyl-4-(2-pyridyl)imidazole

mp : 96-98°C
IR (Nujol) : 3300, 1720, 1590, 1500, 1260 cm^{-1}
NMR ($CDCl_3$, δ) : 2.62 (3H, s), 3.77 (3H, s), 3.86 (3H, s), 6.18 (1H, d, J = 8Hz), 6.9-7.1 (1H, m), 7.39 (1H, dd, J = 2Hz, 8Hz), 7.44 (1H, s), 7.5-7.7 (2H, m), 8.40 (1H, d, J = 5Hz)

Example 56

2-(3,4-Dimethoxyphenyl)-4-(2-pyridyl)imidazole mp : 80-82°C
IR (Nujol) : 1680, 1590, 1490 cm^{-1}
NMR ($CDCl_3$, δ) : 3.83 (3H, s), 3.87 (3H, s), 6.81 (1H, d, J=8Hz), 7.0-7.2 (1H, m), 7.36 (1H, dd, J=2Hz, 8Hz), 7.48 (1H, d, J=2Hz), 7.60 (1H, s), 7.6-7.8 (2H, m), 8.42 (1H, d, J=6Hz)
Mass (m/e) : 281 (M^+)

Example 57 2-(3,4-Dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 234-236°C
IR (Nujol) : 1600 cm^{-1}
NMR ($CDCl_3$-CD_3OD, δ) : 2.50 (3H, s), 3.86 (3H, s), 3.91 (3H, s), 6.86 (1H, d, J=8Hz), 7.3-7.7 (4H, m), 8.42 (2H, d, J=6Hz)

Example 58 2-(3,4-Dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole

mp : 181-182°C (dec.)
IR (Nujol) : 1595, 1530, 1410 cm^{-1}
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 2.85 (2H, q, J=7.5Hz), 3.83 (6H, s), 6.77 (1H, d, J=9Hz), 7.37 (1H, dd, J=2Hz, 9Hz), 7.49 (1H, d, J=2Hz), 7.54, 8.44 (4H, ABq, J=6Hz)
Mass (m/e) : 309(M^+)

Example 59 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(2-pyridyl)imidazole

mp : 118-120°C
IR (Nujol) : 3260, 1610, 1580, 1490 cm^{-1}
NMR ($CDCl_3$, δ) : 2.64 (3H, s), 3.84 (3H, s), 4.01 (3H, s), 6.53 (1H, s), 6.57 (1H, dd, J=2Hz, 9Hz), 7.01 (1H, dd, J=6Hz, 10Hz), 7.5-7.8 (2H, m), 8.23 (1H, d, J=10Hz), 8.50 (1H, d, J=6Hz)

Example 60 2-(3,4-Dimethoxyphenyl)-5-ethyl-4-(2-pyridyl)imidazole

mp : 160-163°C
IR (Nujol) : 1590, 1500, 1270, 1015 cm^{-1}
NMR ($CDCl_3$, δ) : 1.35 (3H, t, J=8Hz), 2.99 (2H, t, J=8Hz), 3.85 (6H, s), 6.80 (1H, d, J=9Hz), 6.9-7.1 (1H, m), 7.33 (1H, dd, J=2Hz, 9Hz), 7.43 (1H, d, J=2Hz), 7.5-7.7 (2H, m), 8.43 (1H, d, J=5Hz)

Example 61 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 224-226°C
IR (Nujol) : 1605 cm^{-1}
NMR (DMSO-d_6, δ) : 2.56 (3H, s), 3.85 (3H, s), 3.96 (3H, s), 6.6-6.8 (2H, m), 7.73 (2H, d, J=6Hz), 8.07 (1H, d, J=9Hz), 8.58 (2H, d, J=6Hz), 11-12 (1H, br s)

Example 62 2-(2,4-Dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole

mp : 212-213°C
IR (Nujol) : 1595, 1530, 1505 cm^{-1}
NMR ($CDCl_3$, δ) : 1.36 (3H, t, J=8Hz), 2.93 (2H, q, J=8Hz), 3.83 (3H, s), 3.97 (3H, s), 6.51 (1H, d, J=2Hz), 6.57 (1H, dd, J=2Hz, 10Hz), 7.52 (2H, dd, J=2Hz, 6Hz), 8.23 (1H, d, J=10Hz), 8.50 (1H, dd, J=2Hz, 6Hz)
Mass (m/e) : 309 (M^+)

Example 63 2-(2-Methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 198-200°C
IR (Nujol) : 1600, 1585, 1560 cm^{-1}
NMR (DMSO-d_6, δ) : 2.55 (3H, s), 3.99 (3H, s), 7.6-6.9 (4H, m), 8.0-8.3 (2H, m), 8.46 (1H, dd, J=2Hz, 5Hz), 8.98 (1H, d, J=2Hz), 11.7 (1H, br s)

Example 64 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 164-166°C
IR (Nujol) : 1615, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.80 (3H, s), 3.93 (3H, s), 6.64 (1H, dd, J=2Hz, 8Hz), 6.68 (1H, d, J=2Hz), 7.40 (1H, dd, J=5Hz, 8Hz), 7.9-8.2 (2H, m), 8.43 (1H, br d, J=5Hz), 8.94 (1H, br s), 11.5 (1H, br s)

Example 65 2-(2,4-Dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole

mp : 148-151°C
IR (Nujol) : 1618, 1590, 1495 cm^{-1}
NMR (DMSO-d_6, δ) : 1.25 (3H, t, J=8Hz), 2.85 (2H, q, J=8Hz), 3.80 (3H, s), 3.91 (3H, s), 6.49-6.65 (2H, m), 6.63 (1H, s), 7.35 (1H, dd, J=8Hz, 4Hz), 7.82-8.01 (2H, m), 8.35 (1H, m), 8.79 (1H, br s)

Example 66 2-(2,5-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 152-154°C
IR (Nujol) : 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.78 (3H, s), 3.91 (3H, s), 6.88 (1H, dd, J = 8Hz, 2Hz), 7.10 (1H, d, J = 8Hz), 7.40 (1H, dd, J = 4Hz, 8Hz), 7.68 (1H, d, J = 2Hz), 8.07 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.44 (1H, br d, J = 4Hz), 8.97 (1H, br s)

Example 67 2-(2,3-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 125-127°C
IR (Nujol) : 1590, 1555 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.77 (3H, s), 3.84 (3H, s), 6.96 (1H, dd, J = 8Hz, 2Hz), 7.06 (1H, dd, J = 8Hz, 8Hz), 7.32 (1H, dd, J = 8Hz, 4Hz), 7.54 (1H, dd, J = 2Hz, 8Hz), 7.97 (1H, ddd, J = 2Hz, 2Hz, 8Hz), 8.33 (1H, br d, J = 4Hz), 8.83 (1H, br s), 11.73 (1H, br s)

Example 68 2-(2,3,4-Trimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 144-146°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.78 (3H, s), 3.81 (3H, s), 3.83 (3H, s), 6.84 (1H, d, J = 9Hz), 7.32 (1H, dd, J = 8Hz, 4Hz), 7.62 (1H, d, J = 9Hz), 7.96 (1H, br d, J = 8Hz), 8.32 (1H, br d, J = 4Hz), 8.82 (1H, br s), 11.62 (1H, br s)

Example 69 2-(3,4,5-Trimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 258-260°C
IR (Nujol) : 1590 cm^{-1}
NMR ($CDCl_3$-CD_3OD, δ) : 2.45 (3H, s), 3.84 (3H, s), 3.90 (6H, s), 7.18 (2H, s), 7.33 (1H, dd, J = 8Hz, 5Hz), 7.96 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.34 (1H, br d, J = 5Hz), 8.72 (1H, br s)

Example 70 2-(4-Chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 145-147°C
IR (Nujol) : 1585, 1595 cm^{-1}
NMR (DMSO-d_6, δ) : 2.54 (3H, s), 4.01 (3H, s), 7.12 (1H, dd, J = 8Hz, 2Hz), 7.25 (1H, d, J = 2Hz), 7.43 (1H, dd, J = 8Hz, 5Hz), 8.08 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.16 (1H, d, J = 8Hz), 8.47 (1H, dd, J = 2Hz, 5Hz), 8.99 (1H, d, J = 2Hz), 11.75 (1H, br s)

Example 71 2-(4-Acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 239-240°C
IR (Nujol) : 3400, 1680, 1590, 1520, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.14 (3H, s), 2.50 (3H, s), 3.91 (3H, s), 7.35 (1H, dd, J = 5Hz, 8Hz), 7.63 (1H, s),

8.02 (1H, s), 8.02 (1H, dt, J = 2Hz, 8Hz), 8.35 (1H, dd, J = 2Hz, 5Hz), 8.82 (1H, d, J = 2Hz), 9.40 (1H, s), 11.63 (1H, s)
Mass (m/e) : 356 (M^+)

Example 72 2-(4-Acetamido-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 215-218°C
IR (Nujol) : 1675, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.06 (3H, s), 2.49 (3H, s), 3.90 (3H, s), 7.14 (1H, dd, J = 8Hz, 2Hz), 7.33 (1H, dd, J = 8Hz, 5Hz), 7.48 (1H, d, J = 2Hz), 7.92 (1H, d, J = 8Hz), 7.96 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.33 (1H, br d, J = 5Hz), 8.82 (1H, br s), 9.99 (1H, s), 11.45 (1H, br s)

Example 73

2-Phenyl-5-methyl-4-(3-pyridyl)imidazole
mp : 206-208°C
IR (Nujol) : 1600, 1590, 1575 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 7.2-7.6 (4H, m), 7.8-8.1 (3H, m), 8.35 (1H, br d, J = 4Hz), 8.83 (1H, br s), 12.39 (1H, br s)

Example 74 2-(2-Methoxy-4-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 203-207°C
IR (Nujol) : 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 2.58 (3H, s), 4.11 (3H, s), 7.37 (1H, m), 7.75-8.14 (4H, m), 8.37 (1H, m), 8.88 (1H, br s), 11.93 (1H, br s)

Example 75 2-(2-Methoxy-4-methylthiophenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 153-156°C
IR (Nujol) : 1600, 1580, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 2.52 (3H, s), 3.94 (3H, s), 6.89 (1H, dd, J = 8Hz, 2Hz), 6.94 (1H, d, J = 2Hz), 7.34 (1H, dd, J = 8Hz, J = 4Hz), 7.96 (1H, d, J = 8Hz), 7.98 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.34 (1H, dd, J = 4Hz, 2Hz), 8.84 (1H, d, J = 2Hz), 11.45 (1H, br s)

Example 76 2-(2,4-Dimethoxyphenyl)-5-hydroxymethyl-4-(3-pyridyl)imidazole

mp : 192-195°C
IR (Nujol) : 1615, 1595 cm^{-1}
NMR (DMSO-d_6, δ) : 3.83 (3H, s), 3.97 (3H, s), 4.70 (2H, br s), 5.26 (1H, br s), 6.66 (1H, dd, J = 7Hz, 2Hz), 6.74 (1H, d, J = 2Hz), 7.24 (1H, dd, J = 5Hz, 8Hz), 7.9-8.3 (2H, m), 8.47 (1H, dd, J = 2Hz, 5Hz), 9.02 (1H, br s)

Example 77 2-(2-Methoxy-4-methylthiophenyl)-5-hydroxymethyl-4-(3-pyridyl)imidazole

mp : 199-201°C
IR (Nujol) : 1605, 1590, 1575 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 3.94 (3H, s), 4.61 (2H, d, J=4Hz), 5.20 (1H, br t, J=4Hz), 6.88 (1H, dd, J=8Hz, 2Hz), 6.93 (1H, d, J=2Hz), 7.35 (1H, dd, J=8Hz, 4Hz), 7.97 (1H, d, J=8Hz), 8.06 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.37 (1H, br d, J=4Hz), 8.90 (1H, br s), 11.57 (1H, br s)

Example 78 2-(4-Amino-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 178-180°C
IR (Nujol) : 3480, 3280, 3150, 1630, 1600, 1560 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.87 (3H, s), 5.58 (2H, s), 6.52 (1H, s), 7.32 (1H, dd, J=5Hz, 8Hz), 7.80 (1H, s), 7.98 (1H, d t, J=2Hz, 8Hz), 8.34 (1H, dd, J=2Hz, 5Hz), 8.82 (1H, d, J=2Hz), 11.30 (1H br s)
Mass (m/e) : 314 (M^+)

Example 79 2-(4-Amino-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 95-100°C
IR (Nujol) : 1615 cm^{-1}
NMR (DMSO-$_6$, δ) : 2.45 (3H, s), 3.83 (3H, s), 5.32 (2H, br s), 6.18 (1H, dd, J=8Hz, 2Hz), 6.24 (1H, d, J=2Hz), 7.30 (1H, dd, J=8Hz, 4Hz), 7.67 (1H, d, J=8Hz), 7.94 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.30 (1H, dd, J=4Hz, 2Hz), 8.80 (1H, d, J=2Hz), 11.13 (1H, br s)

Example 80 2-(2,4-Dimethoxyphenyl)-1,5-dimethyl-4-(3-pyridyl)imidazole

mp : 129-131°C
IR (Nujol) : 1615, 1595, 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 2.40 (3H, s), 3.30 (3H, s), 3.76 (3H, s), 3.80 (3H, s), 6.4-6.7 (2H, m), 7.20 (1H, d, J=8Hz), 7.31 (1H, dd, J=4Hz, 8Hz), 7.89 (1H, br d, J=8Hz), 8.32 (1H, br d, J=4Hz), 8.74 (1H, br s)

Example 81 2-(2-Methoxy-4-methylphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 125-128°C
IR (Nujol) : 1615, 1590 cm^{-1}

Example 82 2-(3-Methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 226-228°C
IR (Nujol) : 1605, 1570 cm^{-1}

Example 83 2-(2,6-Dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 185-187°C
IR (Nujol) : 1608, 1590 cm^{-1}

Example 84 2-(3-Methoxy-4-methylthiophenyl)-4-methyl-5-(4-pyridyl)imidazole

mp : 283-285°C
IR (Nujol) : 1600 cm^{-1}

Example 85 2-(2-Methoxy-4-methylthiophenyl)-4-methyl-5-(4-pyridyl)imidazole

mp : 192-194°C
IR (Nujol) : 1606, 1565 cm^{-1}

Example 86

4-Methyl-2-(2-nitrophenyl)-5-(3-pyridyl)imidazole
mp : 229-230°C
IR (Nujol) : 1613, 1601, 1578, 1539, 1497 cm^{-1}

Example 87

4-Methyl-2-(o-tolyl)-5-(3-pyridyl)imidazole
mp : 129-130°C
IR (Nujol) : 1604, 1570, 1494 cm^{-1}

Example 88

2-(4-Chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole
mp : 229-231°C
IR (Nujol) : 1600, 1574, 1492 cm^{-1}

Example 89 2-[4-(N-Acetyl-N-methylamino)-5-chloro-2-methoxyphenyl]-4-methyl-5-(3-pyridyl)imidazole

mp : 220-221°C
IR (Nujol) : 1672, 1599, 1563, 1525, 1490 cm^{-1}

Example 90

2-(2-Chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole
mp : 108-109°
IR (Nujol) : 1590, 1562, 1480 cm^{-1}

Example 91 2-(3,4-Dichlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp: 269°C
IR (Nujol) : 1600, 1574 cm^{-1}

Example 92

2-(4-Fluorophenyl)-4-methyl-5-(3-pyridyl) imidazole
mp : 123-124°C
IR (Nujol) : 1600, 1570, 1539, 1502 cm^{-1}

Example 93

2-(3-Chlorophenyl)-4-methyl-5-(3-pyridyl) imidazole
mp : 242-243°C
IR (Nujol) : 1607, 1587, 1574, 1489 cm^{-1}

Example 94

2-(2-Fluorophenyl)-4-methyl-5-(3-pyridyl) imidazole
mp : 194-195°C
IR (Nujol) : 1599, 1590, 1567, 1525, 1485 cm^{-1}

Example 95 2-(2,4-Dichlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 160-161°
IR (Nujol) : 1590, 1569, 1556, 1484 cm^{-1}

Example 96 2-(5-Chloro-2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 241-244°C
IR (Nujol) : 1610, 1590, 1565 cm^{-1}

Example 97 2-(5-Chloro-2-methoxy-4-methylphenyl)-4-m thyl-5-(3-pyridyl)imidazole

mp : 185-187°C
IR (Nujol) : 1600, 1580, 1560 cm^{-1}

Example 98

2-(4-Methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole
mp : 199-201°C
IR (Nujol) : 1615, 1600 cm^{-1}

Example 99 4-Methyl-5-(3-pyridyl)-2-(2,4,6-trimethoxyphenyl)imidazole

mp : 65-75°C
IR (Nujol) : 1610, 1590 cm^{-1}

Example 100 4-Methyl-5-(3-pyridyl)-2-(2,4,5-trimethoxyphenyl)imidazole

mp : 189-191°C
IR (Nujol) : 1615, 1600 cm^{-1}

Example 101 2-(4-Benzyloxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 160-162°C
IR (Nujol) : 1615, 1590 cm^{-1}

Example 102 2-(4-Ethoxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 151-153°C
IR (Nujol) : 1615, 1590 cm^{-1}

Example 103 2-(5-Chloro-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 193-195°C
IR (Nujol) : 1600, 1586, 1565, 1619 cm^{-1}

Example 104 2-(4-Hydroxy-3-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 278-279°C
IR (Nujol) : 1609, 1575, 1508, 1490 cm^{-1}

Example 105 2-(3-Hydroxy-4-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 267-269°C
IR (Nujol) : 1595, 1574, 1505 cm^{-1}

Example 106 2-(3-Chloro-4,5-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 215-216°C
IR (Nujol) : 1573, 1497 cm^{-1}

Example 107 2-(3-Chloro-4-hydroxy-5-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 251-253°C
IR (Nujol) : 1575, 1504 cm^{-1}

Example 108 4-Methyl-2-(2-methoxy-5-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 220-223°C
IR (Nujol) : 1593, 1534, 1508, 1490 cm^{-1}

Example 109 4-Methyl-2-(2-methoxy-3-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 145-150°C
IR (Nujol) : 1600, 1566, 1535 cm^{-1}

Example 110 2-(2-Methoxy-4-methylsulfinylphenyl)-4-methyl-5-(3-pyridyl)imidazole
IR (Nujol) : 1660, 1600 cm^{-1}

Example 111 2-(2-Methoxy-4-methylsulfonylphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 115-118°C
IR (Nujol) : 1600, 1590 cm^{-1}

Example 112

2-(2-Aminophenyl)-4-methyl-5-(3-pyridyl)imidazole
mp : 221-222°C
IR (Nujol) : 3450, 1618, 1602, 1573, 1600 cm^{-1}

Example 113 2-(5-Amino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 172-173°C
IR (Nujol) : 3430, 1598, 1569, 1530, 1495 cm^{-1}

Example 114 4-Methyl-2-(4-methylamino-2-methoxyphenyl)-5-(3-pyridyl)imidazole

mp : 54-56°C
IR (Nujol) : 1612, 1580, 1560 cm^{-1}

Example 115 2-(2-Acetamidophenyl)-4-methyl-5-(3-pyridyl)-imidazole

mp : 270-271°C
IR (Nujol) : 1700, 1620, 1598, 1580, 1545, 1495 cm^{-1}

Example 116 4-Methyl-2-[2-(3-methylureido)phenyl]-5-(3-pyridyl)imidazole

mp : 230-231°C
IR (Nujol) : 3270, 1684, 1658, 1618, 1589, 1493 cm^{-1}

Example 117 2-(4-Hydroxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 237-240°C
IR (Nujol) : 1610 cm^{-1}

Example 118 2-(5-Bromo-2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 246-248°C
IR (Nujol) : 1600, 1580 cm^{-1}

Example 119 2-(5-Chloro-4-methylamino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 205-206°C
IR (Nujol) : 1616, 1570, 1546, 1498 cm^{-1}

Example 120

To a suspension of 1-hydroxy-2-(3,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.68 g) in methylene chloride (9 ml) was added phosphorus trichloride (0.76 ml) at ambient temperature. The mixture was refluxed for 1 hour, and cooled. The mixture was adjusted to pH 7.8 with aqueous sodium carbonate. The organic layer was separated, washed with brine, dried over magnesium sulfate, and evaporated. The residue was triturated with diisopropyl ether to give 2-(3,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.39 g).

mp : 246-248°C
IR (Nujol) : 1600, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.82 (3H, s), 3.85 (3H, s), 7.04 (1H, d, J=9Hz), 7.2-7.7 (3H, m), 8.10 (1H, br d, J=8Hz), 8.45 (1H, br d, J=6Hz), 8.92 (1H, br s)

Example 121

To a solution of 1-hydroxy-2-(2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.5 g) in N,N-dimethylformamide (10 ml) was added phosphorus trichloride (0.31 ml) under ice-cooling. The mixture was stirred for 2 hours at 5 to 10°C. The mixture was poured into water (100 ml), and neutralized with aqueous sodium bicarbonate. The precipitate was collected,washed with water, and dried to give 2-(2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (0.31 g).

mp : 198-200°C
IR (Nujol) : 1600, 1585, 1560 cm^{-1}
NMR (DMSO-d_6, δ) : 2.55 (3H, s), 3.99 (3H, s), 6.9-7.6 (4H, m), 8.0-8.3 (2H, m), 8.46 (1H, dd, J=2Hz, 5Hz), 8.98 (1H, d, J=2Hz), 11.7 (1H, br s)

Example 122

To a solution of 1-hydroxy-2-(2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (6.6 g) in N,Ndimethylformamide (130 ml) was added phosphorus trichloride (3.7 ml) under ice-cooling. The mixture was stirred for 2 hours at 5 to 10°C. The reaction mixture was poured into water, neutralized with aqueous sodium bicarbonate, and extracted with ethyl acetate. The extract was washed with water, dried, and evaporated. The residue was subjected to column chromatography on silica gel eluting with a mixture of chloroform and methanol (methanol 0% to 15%). The fractions were collected and evaporated to give 2-(2,4-dimethoxypheyl)-5-methyl-4-(3-pyridyl)imidazole (2.82 g).

mp : 164-166°C
IR (Nujol) : 1615, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.80 (3H, s), 3.93 (3H, s), 6.64 (1H, dd, J=2Hz, 8Hz), 6.68 (1H, d, J=2Hz), 7.40 (1H, dd, J=5Hz), 8Hz), 7.9-8.2 (2H, m), 8.43 (1H, br d, J=5Hz), 8.94 (1H, br s), 11.5 (1H, br s)

Other fractions were collect d and evaporated to give 2-(2,4-dimethoxyphenyl)-5-hydroxymethyl-4-(3-pyridyl)imidazole (1.26 g).

mp : 192-195°C
IR (Nujol) : 1615, 1595 cm^{-1}

NMR (DMSO-d_6, δ) : 3.83 (3H, s), 3.97 (3H, s), 4.70 (2H, br s), 5.26 (1H, br s), 6.66 (1H, dd, J = 7Hz, 2Hz), 6.74 (1H, d, J = 2Hz), 7.24 (1H, dd, J = 5Hz, 8Hz), 7.9-8.3 (2H, m) 8.47 (1H, dd, J = 2Hz, 5Hz), 9.02 (1H, br s)

Example 123

To a solution of 1-hydroxy-2-(2-methoxy-4-methylphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.40 g) in N,N-dimethylformamide (28 ml), was added phosphorus trichloride (0.83 ml), and the mixture was stirred for 2 hours at ambient temperature. Then, the solution was poured into water (150 ml), and stirred for an hour at ambient temperature. After neutrallized with aqueous sodium bicarbonate, resulting precipitates were collected by filtration. The precipitates were dried, dissolved in chloroform, and chromatographed on silica gel eluting with a mixture of chloroform and methanol. The fractions were collected, evaporated and triturated in diisopropyl ether to give 2-(2-methoxy-4-methylphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.82 g)

mp : 125-128°C

IR (Nujol) : 1615, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 2.37 (3H, s), 2.51 (3H, s), 3.95 (3H, s), 7.1-6.8 (2H, m), 7.42 (1H, dd, J = 4Hz, J = 8Hz), 8.00 (1H, d, J = 7Hz), 8.06 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.44 (1H, dd, J = 4Hz, J = 2Hz), 8.94 (1H, d, J = 2Hz)

Mass (M/Z) : 279 (M^+)

Example 124

To a solution of 1-hydroxy-2-(3-methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.98 g) in N,N-dimethylformamide (10 ml) was added triethyl phosphite (1.03 ml), and the mixture was stirred at 90°C for 3 hours. Then the solution was poured into water (60 ml) and stirred at ambient temperature for an hour. The resulting precipitates were filtered, washed with water, and recrystallized from ethanol (6 ml) to give 2-(3-methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.58 g).

mp : 226-228°C

IR (Nujol) : 1605, 1570 cm^{-1}

NMR (DMSO-d_6, δ) : 2.43 (3H, s), 2.51 (3H, s), 3.91 (3H, s), 7.18 (1H, d, J = 9Hz), 7.37 (1H, dd, J = 8Hz, J = 4Hz), 7.7-7.45 (2H, m), 8.03 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.38 (1H, dd, J = 4Hz, J = 2Hz), 8.88 (1H, d, J = 2Hz), 12.4 (1H, br s)

Mass (M/Z) : 311 (M^+)

The following compounds (Examples 125 to 183) were obtained according to a similar manner to that of Example 120, 121, 122, 123 or 124.

Example 125 2-(3,4-Dimethoxyphenyl)-5-methyl-4-(2-pyridyl)imidazole

mp : 96-98°C

IR (Nujol) : 3300, 1720, 1590, 1500, 1260 cm^{-1}

NMR ($CDCl_3$, δ) : 2.62 (3H, s), 3.77 (3H, s), 3.86 (3H, s), 6.18 (1H, d, J = 8Hz), 6.9-7.1 (1H, m), 7.39 (1H, dd, J = 2Hz, 8Hz), 7.44 (1H, s), 7.5-7.7 (2H, m), 8.40 (1H, d, J = 5Hz)

Example 126

2-(3,4-Dimethoxyphenyl)-4-(2-pyridyl)imidazole

mp : 80-82°C

IR (Nujol) : 1680, 1590, 1490 cm^{-1}

NMR ($CDCl_3$, δ) : 3.83 (3H, s), 3.87 (3H, s), 6.81 (1H, d, J = 8Hz), 7.0-7.2 (1H, m), 7.36 (1H, dd, J = 2Hz, 8Hz), 7.48 (1H, d, J = 2Hz), 7.60 (1H, s), 7.6-7.8 (2H, m), 8.42 (1H, d, J = 6Hz)
Mass (m/e) : 281 (M^+)

Example 127 2-(3,4-Dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 234-236°C
IR (Nujol) : 1600 cm^{-1}
NMR ($CDCl_3$-CD_3OD, δ) : 2.50 (3H, s), 3.86 (3H, s), 3.91 (3H, s), 6.86 (1H, d, J = 8Hz), 7.7-7.3 (4H, m), 8.42 (2H, d, J = 6Hz)

Example 128 2-(3,4-Dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole

mp : 181-182°C (dec.)
IR (Nujol) : 1595, 1530, 1410 cm^{-1}
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J = 7.5Hz), 2.85 (2H, q, J = 7.5Hz), 3.83 (6H, s), 6.77 (1H, d, J = 9Hz), 7.37 (1H, dd, J = 2Hz, 9Hz), 7.49 (1H, d, J = 2Hz), 7.54, 8.44 (4H, ABq, J = 6Hz)
Mass (m/e) : 309 (M^+)

Example 129 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(2-pyridyl)imidazole

mp : 118-120°C
IR (Nujol) : 3260, 1610, 1580, 1490 cm^{-1}
NMR ($CDCl_3$, δ) : 2.64 (3H, s), 3.84 (3H, s), 4.01 (3H, s), 6.53 (1H, s), 6.57 (1H, dd, J = 2Hz, 9Hz), 7.01 (1H, dd, J = 6Hz, 10Hz), 7.5-7.8 (2H, m), 8.23 (1H, d, J = 10Hz), 8.50 (1H, d, J = 6Hz)

Example 130 2-(3,4-Dimethoxyphenyl)-5-ethyl-4-(2-pyridyl)imidazole

mp : 160-163°C
IR (Nujol) : 1590, 1500, 1270, 1015 cm^{-1}
NMR ($CDCl_3$, δ) : 1.35 (3H, t, J = 8Hz), 2.99 (2H, t, J = 8Hz), 3.85 (6H, s), 6.80 (1H, d, J = 9Hz), 6.9-7.1 (1H, :m), 7.33 (1H, dd, J = 2Hz, 9Hz), 7.43 (1H, d, J = 2Hz), 7.5-7.7 (2H, m), 8.43 (1H, d, J = 5Hz)

Example 131 2-(2,4-Dimethoxyphenyl)-5-methyl-4-(4-pyridyl)imidazole

mp : 224-226°C
IR (Nujol) : 1605 cm^{-1}
NMR (DMSO-d_6, δ) : 2.56 (3H, s), 3.85 (3H, s), 3.96 (3H, s), 6.6-6.8 (2H, m), 7.73 (2H, d, J = 6Hz), 8.07 (1H, d, J = 9Hz), 8.58 (2H, d, J = 6Hz), 11-12 (1H, br s)

Example 132 2-(2,4-Dimethoxyphenyl)-5-ethyl-4-(4-pyridyl)imidazole

mp : 212-213°C
IR (Nujol) : 1595, 1530, 1505 cm^{-1}
NMR ($CDCl_3$, δ) : 1.36 (3H, t, J=8Hz), 2.93 (2H, q, J=8Hz), 3.83 (3H, s), 3.97 (3H, s), 6.51 (1H, d, J=2Hz), 6.57 (1H, dd, J=2Hz, 10Hz), 7.52 (2H, dd, J=2Hz, 6Hz), 8.23 (1H, d, J=10Hz), 8.50 (1H, dd, J=2Hz, 6Hz)
Mass (m/e) : 309 (M^+)

Example 133 2-(2,4-Dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole

mp : 148-151°C
IR (Nujol) : 1618, 1590, 1495 cm^{-1}
NMR (DMSO-d_6, δ) : 1.25 (3H, t, J=8Hz), 2.85 (2H, q, J=8Hz), 3.80 (3H, s), 3.91 (3H, s), 6.49-6.65 (2H, m), 6.63 (1H, s), 7.35 (1H, dd, J=8Hz, 4Hz), 7.82-8.01 (2H, m), 8.35 (1H, m), 8.79 (1H, br s)

Example 134 2-(2,5-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 152-154°C
IR (Nujol) : 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.78 (3H, s), 3.91 (3H, s), 6.88 (1H, dd, J=8Hz, 2Hz), 7.10 (1H, d, J=8Hz), 7.40 (1H, dd, J=4Hz, 8Hz), 7.68 (1H, d, J=2Hz), 8.07 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.44 (1H, br d, J=4Hz), 8.97 (1H, br s)

Example 135 2-(2,3-Dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 125-127°C
IR (Nujol) : 1590, 1555 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.77 (3H, s), 3.84 (3H, s), 6.96 (1H, dd, J=8Hz, 2Hz), 7.06 (1H, dd, J=8Hz, 8Hz), 7.32 (1H, dd, J=8Hz, 4Hz), 7.54 (1H, dd, J=2Hz, 8Hz), 7.97 (1H, ddd, J=2Hz, 2Hz, 8Hz), 8.33 (1H, br d, J=4Hz), 8.83 (1H, br s), 11.73 (1H, br s)

Example 136 2-(2,3,4-Trimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 144-146°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.78 (3H, s), 3.81 (3H, s), 3.83 (3H, s), 6.84 (1H, d, J=9Hz), 7.32 (1H, dd, J=8Hz, 4Hz), 7.62 (1H, d, J=9Hz), 7.96 (1H, br d, J=8Hz), 8.32 (1H, br d, J=4Hz), 8.82 (1H, br s), 11.62 (1H, br s)

Example 137 2-(3,4,5-Trimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 258-260°C
IR (Nujol) : 1590 cm^{-1}
NMR ($CDCl_3$-CD_3OD, δ) : 2.45 (3H, s), 3.84 (3H, s), 3.90 (6H, s), 7.18 (2H, s), 7.33 (1H, dd, J=8Hz, 5Hz), 7.96 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.34 (1H, br d, J=5Hz), 8.72 (1H, br s)

Example 138 2-(4-Chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 145-147°C
IR (Nujol) : 1585, 1595 cm^{-1}
NMR (DMSO-d_6, δ) : 2.54 (3H, s), 4.01 (3H, s), 7.12 (1H, dd, J=8Hz, 2Hz), 7.25 (1H, d, J=2Hz), 7.43 (1H, dd, J=8Hz, 5Hz), 8.08 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.16 (1H, d, J=8Hz), 8.47 (1H, dd, J=2Hz, 5Hz), 8.99 (1H, d, J=2Hz), 11.75 (1H, br s)

Example 139 2-(4-Acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 239-240°C
IR (Nujol) : 3400, 1680, 1590, 1520, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.14 (3H, s), 2.50 (3H, s), 3.91 (3H, s), 7.35 (1H, dd, J=5Hz, 8Hz), 7.63 (1H, s), 8.02 (1H, s), 8.02 (1H, dt, J=2Hz, 8Hz), 8.35 (1H, dd, J=2Hz, 5Hz), 8.82 (1H, d, J=2Hz), 9.40 (1H, s), 11.63 (1H, s)
Mass (m/e) : 356 (M^+)

Example 140 2-(4-Acetamido-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 215-218°C
IR (Nujol) : 1675, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.06 (3H, s), 2.49 (3H, s), 3.90 (3H, s), 7.14 (1H, dd, J=8Hz, 2Hz), 7.33 (1H, dd, J=8Hz, 5Hz), 7.48 (1H, d, J=2Hz), 7.92 (1H, d, J=8Hz), 7.96 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.33 (1H, br d, J=5Hz), 8.82 (1H, br s), 9.99 (1H, s), 11.45 (1H, br s)

Example 141

2-Phenyl-5-methyl-4-(3-pyridyl)imidazole
mp : 206-208°C
IR (Nujol) : 1600, 1590, 1575 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 7.2-7.6 (4H, m), 7.8-8.1 (3H, m), 8.35 (1H, br d, J=4Hz), 8.83 (1H, br s), 12.39 (1H, br s)

Example 142 2-(2-Methoxy-4-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 203-207°C
IR (Nujol) : 1580 cm^{-1}
NMR (DMSO-d_6, δ) : 2.58 (3H, s), 4.11 (3H, s), 7.37 (1H, m), 7.75-8.14 (4H, m), 8.37 (1H, m), 8.88 (1H, br s), 11.93 (1H, br s)

Example 143 2-(2-Methoxy-4-methylthiophenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 153-156°C
IR (Nujol) : 1600, 1580, 1565 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 2.52 (3H, s), 3.94 (3H, s), 6.89 (1H, dd, J = 8Hz, J = 2Hz), 6.94 (1H, d, J = 2Hz), 7.34 (1H, dd, J = 8Hz, J = 4Hz), 7.96 (1H, d, J = 8Hz), 7.98 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.34 (1H, dd, J = 4Hz, J = 2Hz), 8.84 (1H, d, J = 2Hz), 11.45 (1H, br s)

Example 144 2-(2-Methoxy-4-methylthiophenyl)-5-hydroxymethyl-4-(3-pyridyl)imidazole

mp : 199-201°C
IR (Nujol) : 1605, 1590, 1575 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 3.94 (3H, s), 4.61 (2H, d, J = 4Hz), 5.20 (1H, br t, J = 4Hz), 6.88 (1H, dd, J = 8Hz, 2Hz), 6.93 (1H, d, J = 2Hz), 7.35 (1H, dd, J = 8Hz, J = 4Hz), 7.97 (1H, d, J = 8Hz), 8.06 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.37 (1H, br d, J = 4Hz), 8.90 (1H, br s), 11.57 (1H, br s)

Example 145 2-(4-Amino-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 178-180°C
IR (Nujol) : 3480, 3280, 3150, 1630, 1600, 1560 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.87 (3H, s), 5.58 (2H, s), 6.52 (1H, s), 7.32 (1H, dd, J = 5Hz, 8Hz), 7.80 (1H, s), 7.98 (1H, dt, J = 2Hz, 8Hz), 8.34 (1H, dd, J = 2Hz, 5Hz), 8.82 (1H, d, J = 2Hz), 11.30 (1H, br s)
Mass (m/e) : 314 (M^+)

Example 146 2-(4-Amino-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole

mp : 95-100°C
IR (Nujol) : 1615 cm^{-1}
NMR (DMSO-d_6, δ) : 2.45 (3H, s), 3.83 (3H, s), 5.32 (2H, br s), 6.18 (1H, dd, J = 8Hz, 2Hz), 6.24 (1H, d, J = 2Hz), 7.30 (1H, dd, J = 8Hz, 4Hz), 7.67 (1H, d, J = 8Hz), 7.94 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.30 (1H, dd, J = 4Hz, 2Hz), 8.80 (1H, d, J = 2Hz), 11.13 (1H, br s)

Example 147 2-(2,6-Dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 185-187°C
IR (Nujol) : 1608, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.44 (3H, s), 3.72 (6H, s), 6.74 (2H, d, J = 8Hz), 7.55-7.25 (2H, m), 7.98 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.38 (1H, dd, J = 5Hz, J = 2Hz), 8.85 (1H, d, J = 2Hz), 11.9 (1H, br s)
Mass (M/Z) : 295 (M^+)

Example 148 2-(3-Methoxy-4-methylthiophenyl)-4-methyl-5-(4-pyridyl)imidazole

mp : 283-285°C
IR (Nujol) : 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.43 (3H, s), 2.53 (3H, s), 3.93 (3H, s), 7.22 (1H, d, J = 8Hz), 7.8-7.4 (4H, m), 8.54 (2H, d, J = 8Hz), 12.50 (1H, br s)
Mass (M/Z) : 311 (M^+)/

Example 149 2-(2-Methoxy-4-methylthiophenyl)-4-methyl-5-(4-pyridyl)imidazole

mp : 192-194°C
IR (Nujol) : 1606, 1565 cm^{-1} NMR (DMSO-d_6, δ) : 2.56 (3H, s), 2.58 (3H, s), 4.00 (3H, s), 6.99 (1H, dd, J = 9Hz, J = 2Hz), 7.04 (1H, d, J = 2Hz), 7.73 (2H, d, J = 6Hz), 8.09 (1H, d, J = 9Hz), 8.57 (2H, d, J = 6Hz), 11.55 (1H, br s)
Mass (M/Z) : 311 (M^+)

Example 150

4-Methyl-2-(2-nitrophenyl)-5-(3-pyridyl)imidazole
mp : 229-230°C
IR (Nujol) : 1613, 1601, 1578, 1539, 1497 cm^{-1}
NMR (DMSO-d_6, δ) : 2.51 (3H, s), 7.40 (1H, dd, J = 8Hz, 5Hz), 7.54-8.06 (5H, m), 8.45 (1H, dd, J = 5Hz, J = 2Hz), 8.87 (1H, d, J = 2Hz), 12.7 (1H, br s)
Mass (M/Z) : 280 (M^+)

Example 151

4-Methyl-2-(δ -tolyl)-5-(3-pyridyl)imidazole
mp : 129-130°C
IR (Nujol) : 1604, 1570, 1494 cm^{-1}
NMR (DMSO-d_6, δ) : 2.57 (3H, s), 2.72 (3H, s), 7.3-7.9 (5H, m), 8.18 (1H, ddd, J = 8Hz, 2Hz,2Hz), 8.52 (1H, dd, J = 5Hz, 2Hz), 9.08 (1H, d, J = 2Hz)
Mass (M/Z) : 249 (M^+)

Example 152 2-(4-Chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 229-231°C
IR (Nujol) : 1600, 1574, 1492 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 7.32-7.58 (3H, m), 7.89-8.13 (3H, m), 8.43 (1H, dd, J=5Hz, 2Hz), 8.88 (1H, d, J=2Hz)
Mass (M/Z) : 269 (M^+)

Example 153 2-[4-(N-Acetyl-N-methylamino)-5-chloro-2-methoxyphenyl]-4-methyl-5-(3-pyridyl)imidazole

mp : 220-221°C
IR (Nujol) : 1672, 1599, 1563, 1525, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 2.79 (3H, s), 3.14 (3H, s), 4.01 (3H, s), 7.28-7.56 (2H, m), 7.95-8.26 (2H, m), 8.44 (1H, dd, J=5Hz, 2Hz), 8.91 (1H, d, J=2Hz)
Mass (M/Z) : 370 (M^+)

Example 154 2-(2-Chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 108-109°C
IR (Nujol) : 1590, 1562, 1480 cm^{-1}
NMR (DMSO-d_6, δ) : 2.51 (3H, s), 7.25-7.9 (5H, m), 8.09 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.43 (1H, dd, J=5Hz, 2Hz), 8.92 (1H, d, J=2Hz), 12.2 (1H, br s)
Mass (M/Z) : 269 (M^+)

Example 155 2-(3,4-Dichlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 269°C
IR (Nujol) : 1600, 1574 cm^{-1}
NMR (DMSO-d_6, δ) : 2.51 (3H, s), 7.46 (1H, dd, J=8Hz, 5Hz), 7.71 (1H, d, J=8Hz), 7.8-8.25 (3H, m), 8.45 (1H, d, J=5Hz), 8.93 (1H, s), 12.68 (1H, br s)
Mass (M/Z) : 303 (M-1)

Example 156 2-(4-Fluorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 123-124°C
IR (Nujol) : 1600, 1570, 1539, 1502 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 7.16-7.53 (3H, m), 7.87-8.19 (3H, m), 8.48 (1H, dd, J=5Hz, 2Hz), 8.97 (1H, d, J=2Hz)
Mass (M/Z) : 253 (M^+)

Example 157 2-(3-Chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 242-243°C

IR (Nujol) : 1607, 1587, 1574, 1489 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 7.22-7.56 (3H, m), 7.79-8.21 (3H, m), 8.47 (1H, d, J=5Hz), 8.95 (1H, s)
Mass (M/Z) : 269 (M^+)

Example 158 2-(2-Fluorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 194-195°C
IR (Nujol) : 1599, 1590, 1567, 1525, 1485 cm^{-1}
NMR (DMSO-d_6, δ) : 2.60 (3H, s), 7.24-7.63 (4H, m), 7.95-8.36 (2H, m), 8.53 (1H, dd, J=5Hz, 2Hz), 9.08 (1H, d, J=2Hz)
Mass (M/Z) : 253 (M^+)

Example 159 2-(2,4-Dichlorophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 160-161°C
IR (Nujol) : 1590, 1569, 1556, 1484 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 7.38 (1H, dd, J=8Hz, 5Hz), 7.49 (1H, dd, J=8Hz, 2Hz), 7.69 (1H, d, J=2Hz), 7.83 (1H, d, J=8Hz), 8.04 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.43 (1H, d, J=5Hz), 8.91 (1H, s), 12.46 (1H, br s)
Mass (M/Z) : 303 (M-1)

Example 160 2-(5-Chloro-2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 241-244°C
IR (Nujol) : 1610, 1590, 1565 cm^{-1}
NMR ($CDCl_3$-CD_3OD δ) : 2.50 (3H, s), 3.86 (3H, s), 3.94 (3H, s), 6.61 (1H, s), 7.38 (1H, dd, J=8Hz, J=4Hz), 8.2-7.8 (2H, m), 8.36 (1H, br d, J=4Hz), 8.74 (1H, br s)
Mass (M/Z) : 329 (M^+)

Example 161 2-(5-Chloro-2-methoxy-4-methylphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 185-187°C
IR (Nujol) : 1600, 1580, 1560 cm^{-1}
NMR (DMSO-d_6, δ) : 2.37 (3H, s), 2.52 (3H, s), 3.94 (3H, s), 7.13 (1H, s), 7.36 (1H, dd, J=8Hz, J=4Hz), 8.00 (1H, s), 8.03 (1H, ddd, J=2Hz, J=2Hz, J=8Hz), 8.37 (1H, dd, J=2Hz, J=4Hz), 8.87 (1H, d, J=2Hz), 11.63 (1H, br s)
Mass (M/Z) : 313 (M^+)

Example 162 2-(4-Methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 199-201°C
IR (Nujol) : 1615, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.51 (3H, s), 3.83 (3H, s), 7.05 (2H, d, J=9Hz), 7.42 (1H, dd, J=5Hz, J=8Hz), 7.8-8.2 (3H, m), 8.45 (1H, dd, J=5Hz, J=2Hz), 8.94 (1H, d, J=2Hz), 12.1 (1H, br s)
Mass (M/Z) : 265 (M^+)

Example 163 4-Methyl-5-(3-pyridyl)-2-(2,4,6-trimethoxyphenyl)imidazole

mp : 65-75°C
IR (Nujol) : 1610, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.42 (3H, s), 3.69 (3H, s), 3.83 (3H, s), 6.28 (2H, s), 7.33 (1H, dd, J=8Hz, J=4Hz), 7.93 (1H, br d J=8Hz), 8.32 (1H, br d, J=4Hz), 8.80 (1H, br s)
Mass (M/Z) : 325 (M^+)

Example 164 4-Methyl-5-(3-pyridyl)-2-(2,4,5-trimethoxyphenyl)imidazole

mp : 189-191°C
IR (Nujol) : 1615, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.76 (3H, s), 3.83 (3H, s), 3.93 (3H, s), 6.74 (1H, s), 7.35 (1H, dd, J=8Hz, J=4Hz), 7.60 (1H, s), 7.99 (1H, ddd, J=2Hz, 2Hz, 8Hz), 8.46 (1H, dd, J=2Hz, J=4Hz), 8.85 (1H, d, J=2Hz)
Mass (M/Z) : 325 (M^+)

Example 165 2-(4-Benzyloxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 160-162°C
IR (Nujol) : 1615, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.48 (3H, s), 3.92 (3H, s), 5.14 (2H, s), 6.69 (1H, dd, J=8Hz, J=2Hz), 6.74 (1H, d, J=2Hz), 7.6-7.2 (6H, m), 8.1-7.8 (2H, m), 8.36 (1H, br d, J=4Hz), 8.86 (1H, br s)
Mass (M/Z) : 371 (M^+)

Example 166 2-(4-Ethoxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 151-153°C
IR (Nujol) : 1615, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 1.36 (3H, t, J=7Hz), 2.53 (3H, s), 3.94 (3H, s), 4.10 (2H, q, J=7Hz), 6.63 (1H, dd, J=2Hz, J=7Hz), 6.68 (1H, d, J=2Hz), 7.41 (1H, dd, J=8Hz, J=4Hz), 7.8-8.3 (2H, m), 8.42 (1H, d, J=4Hz), 8.95 (1H, br s), 11.50 (1H, br s)
Mass (M/Z) : 309 (M^+)

Example 167 2-(5-Chloro-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 193-195°C
IR (Nujol) : 1600, 1586, 1565, 1619 cm^{-1}
NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.95 (3H, s), 7.11 (1H, d, J=8Hz), 7.21-7.48 (2H, m), 7.89-8.13 (2H, m), 8.39 (1H, d, J=5Hz), 8.88 (1H, s), 11.72 (1H, br s)
Mass (M/Z) : 298 (M^+)

Example 168 2-(4-Hydroxy-3-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 278-279°C
IR (Nujol) : 1609, 1575, 1508, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.43 (3H, s), 3.83 (3H, s), 6.79 (1H, d, J=8Hz), 7.2-7.55 (3H, m), 7.97 (1H, d, J=8Hz), 8.35 (1H, s), 8.83 (1H, s), 9.13 (1H, s)
MASS (M/Z) : 281 (M^+)

Example 169 2-(3-Hydroxy-4-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 267-269°C
IR (Nujol) : 1595, 1574, 1505 cm^{-1}
NMR (DMSO-d_6, δ) : 2.45 (3H, s), 3.82 (3H, s), 7.00 (1H, d, J=8Hz), 7.26-7.56 (3H, m), 8.05 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.40 (1H, dd, J=5Hz, 2Hz), 8.86 (1H, d, J=2Hz), 9.08 (1H, s), 12.10 (1H, br s)
MASS (M/Z) : 281 (M^+)

Example 170 2-(3-Chloro-4,5-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 215-216°C
IR (Nujol) : 1573, 1497 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.90 (3H, s), 3.96 (3H, s), 7.42 (1H, dd, J=8Hz, 5Hz), 7.67 (2H, s), 8.10 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.47 (1H, dd, J=5Hz, 2Hz), 8.93 (1H, d, J=2Hz)
Mass (M/Z) : 329 (M^+)

Example 171 2-(3-Chloro-4-hydroxy-5-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 251-253°C
IR (Nujol) : 1575, 1504 cm^{-1}
NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.93 (3H, s), 7.42 (1H, br s), 7.54 (1H, s), 7.57 (1H, s), 8.05 (1H, d, J=8Hz), 8.42 (1H, s), 8.90 (1H, s), 9.62 (1H, s), 12.33 (1H, br s)
Mass (M/Z) : 315 (M^+)

Example 172 4-Methyl-2-(2-methoxy-5-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 220-223°C
IR (Nujol) : 1593, 1534, 1508, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 4.07 (3H, s), 7.18-7.46 (2H, m), 7.85-8.12 (2H, m), 8.47 (1H, d, J = 5Hz), 8.77-8.91 (2H, m), 11.86 (1H, br s)/
Mass (M/Z) : 310 (M^+)

Example 173 4-Methyl-2-(2-methoxy-3-nitrophenyl)-5-(3-pyridyl)imidazole

mp : 145-150°C
IR (Nujol) : 1600, 1566, 1535 cm^{-1}
NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.78 (3H, s), 7.2-7.5 (2H, m), 7.83 (1H, dd, J = 8Hz, 2Hz), 8.02 (1H, d, J = 8Hz), 8.18 (1H, dd, J = 8Hz, 2Hz), 8.36 (1H, d, J = 5Hz), 8.87 (1H, s), 12.24 (1H, br s)
Mass (M/Z) : 310 (M^+)

Example 174 2-(2-Methoxy-4-methylsulfinylphenyl)-4-methyl-5-(3-pyridyl)imidazole
IR (Nujol) : 1660, 1600 cm^{-1}

Example 175 2-(2-Methoxy-4-methylsulfonylphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 115-118°C
IR (Nujol) : 1600, 1590 cm^{-1}

Example 176

2-(2-Aminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 221-222°C
IR (Nujol) : 3450, 1618, 1602, 1573, 1600 cm^{-1}

Example 177 2-(5-Amino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 172-173°C
IR (Nujol) : 3430, 1598, 1569, 1530, 1495 cm^{-1}

Example 178 4-Methyl-2-(4-methylamino-2-methylphenyl)-5-(3-pyridyl)imidazole

mp : 54-56°C
IR (Nujol) : 1612, 1580, 1560 cm^{-1}

Example 1799 2-(2-Acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 270-271°C
IR (Nujol) : 1700, 1620, 1598, 1580, 1545, 1495 cm^{-1}

Example 180 4-Methyl-2-[2-(3-methylureido)phenyl]-5-(3-pyridyl)imidazole

mp : 230-231°C
IR (Nujol) : 3270, 1684, 1658, 1618, 1589, 1493 cm^{-1}

Example 181 2-(4-Hydroxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 237-240°C
IR (Nujol) : 1610 cm^{-1}

Example 182 2-(5-Bromo-2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 246-248°C
IR (Nujol) : 1600, 1580 cm^{-1}

Example 183 2-(5-Chloro-4-methylamino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole

mp : 205-206°C
IR (Nujol) : 1616, 1570, 1546, 1498 cm^{-1}

Example 184

To a solution of 1-hydroxy-2-(3,4-dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole (1.86 g) in N,N-dimethylformamide (38 ml) was added phosphorus trichloride (0.10 ml) under ice-cooling. The mixture was stirred for 2 hours at 5 to 10°C. The reaction mixture was poured into water, neutralized with aqueous sodium bicarbonate, and extracted with ethyl acetate. The extract was washed with water, dried, and evaporated. The residue was subjected to column chromatography on silica gel eluting with a mixture of chloroform and methanol (methanol 1% to 5%). The fractions were collected and evaporated to give 2-(3,4-dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)imidazole (0.89 g), which was diluted with methanol (8 ml). 1.2 Equivalent of hydrogen chloride gas was bubbled thereinto and diethyl ether was added to the mixture under cooling. The precipitate was collected and dried to give 2-(3,4-dimethoxyphenyl)-4-ethyl-5-(3-pyridyl)-imidazole hydrochloride (0.43 g).

mp : 245-248°C
IR (Nujol) : 1650, 1605, 1515 cm^{-1}
NMR (DMSO-d_6, δ) : 1.33 (3H, t, J = 8Hz), 2.76 (2H, q, J = 8Hz), 3.71 (3H, s), 3.81 (3H, s), 6.82 (1H, d, J = 8Hz), 7.16 (1H, s), 7.10-7.30 (1H, m), 7.72 (1H, dd, J = 8Hz, 4Hz), 8.15 (1H, d, J = 8Hz), 8.45-8.70 (2H, br s)

Example 185

To a solution of 2-(2,4-dimethoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (0.80 g) in N,N-dimethylformamide (12 ml) was added sodium hydride (0.13 g, 60% suspension in oil), and the mixture was stirred for 10 minutes. Then methyl iodide (0.34 ml) was added thereto, and the reaction was stirred at ambient temperature for 5 hours. The solution was poured into water (100 ml), and extracted with ethyl acetate. The extract was washed with water, dried over sodium sulfate, and chromatographed on silica gel (25 g) eluting with chloroform. The fractions were collected and evaporated, and the residue was triturated with a mixture of ethyl acetate and diisopropyl ether (1:1 V/V) to give 2-(2,4-dimethoxyphenyl)-1,5-dimethyl-4-(3-pyridyl)-imidazole (70 mg).

mp : 129-131°C

IR (Nujol) : 1615, 1595, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 2.40 (3H, s), 3.30 (3H, s), 3.76 (3H, s), 3.80 (3H, s), 6.7-6.4 (2H, m), 7.20 (1H, d, J=8Hz), 7.31 (1H, dd, J=4Hz, 8Hz), 7.89 (1H, br d, J=8Hz), 8.32 (1H, br d, J=4Hz), 8.74 (1H, br s)

Example 186

A solution of 2-(2-Aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.7 g) and 2-methylthio-2-imidazoline hydriodide (1.23 g) in N,N-dimethylformamide (10 ml) was stirred at 100°C for 24 hours. The resulting precipitate was collected by filtration, washed with N,N-dimethylformamide and ethylacetate, successively. To a solution of the residue in ethanol (10 ml) was added a solution of 20% hydrogen chloride in ethanol (2 ml) at ambient temperature, and was evaporated under reduced pressure. The precipitate was triturated in ethanol and diethyl ether to give 2-(2-aminophenyl)-1,5-dimethyl-4-(3-pyridyl)imidazole dihydrochloride (0.13 g). mp : 285-286°C

IR (Nujol) : 1587, 1512 cm^{-1}

NMR (D_2O, δ) : 2.59 (3H, s), 4.48 (3H, s), 7.10-7.68 (4H, m), 8.05 (1H, dd, J=8Hz, 6Hz), 8.53-8.76 (2H, m), 8.99 (1H, s)

Mass (M/Z) : 264 (M^+, free)

Example 187

A solution of 2-(4-acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (1.0 g) in 10% hydrochloric acid (30 ml) was stirred at 80 to 85°C for 4 hours. The reaction mixture was poured into water (100 ml) and washed with ethyl acetate. The solution was adjusted to pH 8.0 with 20% potassium carbonate and extracted with ethyl acetate. The extract was washed with brine and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was crystallized from a mixture of ethyl acetate and diethyl ether to give 2-(4-amino-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (0.63 g).

mp : 178-180°C

IR (Nujol) : 3480, 3280, 3150, 1630, 1600, 1560 cm^{-1}

NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.87 (3H, s), 5.58 (2H, s), 6.52 (1H, s), 7.32 (1H, dd, J=5Hz, 8Hz), 7.80 (1H, s), 7.98 (1H, dt, J=2Hz, 8Hz), 8.34 (1H, dd, J=2Hz, 5Hz), 8.82 (1H, d, J=2Hz), 11.30 (1H, br s)

Mass (m/e) : 314 (M^+)

Example 188

A solution of 2-(4-acetamido-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (0.55 g) in 1N-hydrochloric acid (25 ml) was refluxed for 5.5 hours, and cooled. After neutralized with aqueous sodium bicarbonate, the mixture was extracted with chloroform. The extract was dried over sodium sulfate, evaporated, and the residue was triturated with a mixture of methanol and diisopropyl ether to give 2-(4-amino-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole (0.24 g).

mp : 95-100°C

IR (Nujol) : 1615 cm^{-1}

NMR (DMSO-d_6, δ) : 2.45 (3H, s), 3.83 (3H, s), 5.32 (2H, br s), 6.18 (1H, dd, J = 8Hz, 2Hz), 6.24 (1H, d, J = 2Hz), 7.30 (1H, dd, J = 8Hz, 4Hz), 7.67 (1H, d, J = 8Hz), 7.94 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.30 (1H, dd, J = 4Hz, 2Hz), 8.80 (1H, d, J = 2Hz), 11.13 (1H, br s)

Example 189

A solution of 2-[4-(N-acetyl-N-methylamino)-5-chloro-2-methoxyphenyl]-4-methyl-5-(3-pyridyl)imidazole (0.70 g) and conc. hydrochloric acid (7 ml) in a mixture of water (7 ml) and ethanol (7 ml) was refluxed for 7 hours with stirring. After allowed to cool to ambient temperature, the mixture was evaporated under reduced pressure. The resulting oil was poured into water (20 ml). After neutrallized with aqueous potassium bicarbonate the mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. The solvent was distilled off to give 2-(5-chloro-4-methylamino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.58 g).

mp : 205-206°C

IR (Nujol) : 1616, 1570, 1546, 1498 cm^{-1}

NMR (DMSO-d_6, δ) : 2.51 (3H, s), 2.87 (3H, d, J = 6Hz), 3.97 (3H, s), 5.77 (1H, d, J = 6Hz), 6.32 (1H, s), 7.39 (1H, dd, J = 8Hz, 5Hz), 7.92 (1H, s), 8.07 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.40 (1H, d, J = 5Hz), 8.92 (1H, s), 11.38 (1H, br s)

Example 190

To a solution of 2-(2-methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole (1.0 g) in chloroform (50 ml) and ethanol (25 ml), was added a solution of m-chloroperbenzoic acid (0.53 g, 80% pure) in chloroform (5.3 ml) at -30 to -40°C. The mixture was stirred at the same temperature for 4 hours, and then warmed to ambient temperature. The reaction mixture was diluted with chloroform (100 ml) and washed with aqueous sodium bicarbonate and brine successively. After dried over sodium sulfate, the mixture was chromatographed on silica gel eluting with a mixture of chloroform and methanol to give 2-(2-methoxy-4-methylsulfinylphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.82 g).

IR (Nujol) : 1660, 1600 cm^{-1}

NMR ($CDCl_3$, δ) : 2.48 (3H, s), 2.72 (3H, s), 3.98 (3H, s), 7.16 (1H, dd, J = 8Hz, J = 2Hz), 7.25 (1H, dd, J = 8Hz, J = 5Hz), 7.33 (1H, d, J = 2Hz), 7.98 (1H, br d, J = 8Hz), 8.35 (1H, d, J = 8Hz), 8.37 (1H, dd, J = 2Hz, J = 5Hz), 8.84 (1H, br s), 10.68 (1H, br s)

Example 191

To a solution of 2-(2-methoxy-4-methylthiophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.93 g) in acetic acid (10 ml) was added aqueous potassium permanganate (0.80 g in 15 ml) at ambient temperature, and the mixture was stirred at ambient temperature for 3 hours. After neutrallized with aqueous sodium bicarbonate, the mixture was extracted with chloroform. The organic layer was washed with water, dried over sodium sulfate, and concentrated. The residue was chromatographed on silica gel eluting with a mixture of chloroform and methanol to give 2-(2-methoxy-4-methylsulfonylphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.16 g). mp : 115-118°C

IR (Nujol) : 1600, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 2.53 (3H, s), 3.25 (3H, s), 4.05 (3H, s), 7.7-7.2 (3H, m), 7.8-8.5 (3H, m), 8.85 (1H, br s), 11.85 (1H, br s)

Mass (M/Z) : 343 (M^+)

Example 192

A mixture of 4-methyl-2-(2-nitrophenyl)-5-(3-pyridyl)imidazole (4.99 g) and 10% palladium on carbon (1.0 g) in a mixture of tetrahydrofuran (150 ml) and methanol (150 ml) was hydrogenated at ambient temperature under atmospheric pressure of hydrogen gas. After removal of the catalyst by filtration, the filtrate was evaporated under reduced pressure. The residue was recrystallized from ethanol to give 2-(2-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (4.22 g).

mp : 221-222°C

IR (Nujol) : 3450, 1618, 1602, 1573, 1600 cm^{-1}

NMR (DMSO-d_6, δ) : 2.52 (3H, s), 6.54-7.23 (3H, m), 7.45 (1H, dd, J = 8Hz, 5Hz), 7.64 (1H, d, J = 8Hz), 8.10 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.48 (1H, dd, J = 5Hz, 2Hz), 8.95 (1H, d, J = 2Hz)

Mass (M/Z) : 250 (M^+)

Example 193

2-(5-Amino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole was obtained according to a similar manner to that of Example 192.

mp : 172-173°C

IR (Nujol) : 3430, 1598, 1569, 1530, 1495 cm^{-1}

NMR (DMSO-d_6, δ) : 2.49 (3H, s), 3.82 (3H, s), 6.53 (1H, dd, J = 8Hz, 2Hz), 6.83 (1H, d, J = 8Hz), 7.22-7.48 (2H, m), 7.98 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.36 (1H, dd, J = 5Hz, 2Hz), 8.87 (1H, d, J = 2Hz)

Mass (M/Z) : 280 (M^+)

Example 194

A mixture of 2-(5-Chloro-4-methylamino-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.50 g) and 10% palladium on carbon (7.5 g) in a mixture of triethylamine (0.64 ml) and methanol (20 ml) was hydrogenated at ambient temperature under atmospheric pressure of hydrogen gas. After removal of the insoluble substance by filtration, the filtrate was evaporated under reduced pressure. The residue was triturated in diisopropyl ether to give 4-methyl-2-(4-methylamino-2-methoxyphenyl)-5-(3-pyridyl)imidazole (0.10 g).

mp : 54-56°C

IR (Nujol) : 1612, 1580, 1560 cm^{-1}

NMR (DMSO-d_6, δ) : 2.48 (3H, s), 2.75 (3H, d, J = 6Hz), 3.92 (3H, s), 5.94 (1H, d, J = 6Hz), 6.15-6.35 (2H, m), 7.38 (1H, dd, J = 8Hz, 5Hz), 7.81 (1H, d, J = 8Hz), 8.02 (1H, d, J = 8Hz), 8.37 (1H, d, J = 5Hz), 8.88 (1H, s), 11.22 (1H, br s)

Mass (M/Z) : 294 (M^+)

Example 195

A solution of 2-(2-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.5 g) and acetic anhydride (0.38 ml) in acetic acid (5 ml) was stirred at ambient temperature for 1.5 hours. The resulting precipitate was collected by filtration, and recrystallized from ethanol to give 2-(2-acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.55 g).

mp : 270-271°C

IR (Nujol) : 1700, 1620, 1598, 1580, 1545, 1495 cm^{-1}

NMR (DMSO-d_6, δ) : 2.21 (3H, s), 2.52 (3H, s), 7.0-7.6 (3H, m), 7.85 (1H, s), 8.10 (1H, ddd, J = 8Hz, 2Hz, 2Hz), 8.4-8.75 (2H, m), 8.97 (1H, d, J = 2Hz)

Mass (M/Z) : 292 (M^+)

Example 196

A solution of 2-(2-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.5 g) and methylisocyanate (0.15 ml) in a mixture of tetrahydrofuran (5 ml) and methanol (2 ml) was stirred at ambient temperature for 5 hours. The resulting precipitate was collected by filtration, washed with a mixture of ethanol and chloroform and dried in vacuo to give 4-methyl-2-[2-(3-methylureido)phenyl]-5-(3-pyridyl)imidazole (0.51 g).

mp : 230-231°C

IR (Nujol) : 3270, 1684, 1658, 1618, 1589, 1493 cm^{-1}

NMR (D_2O-DCl, δ) : 2.62 (3H, s), 2.70 (3H, s), 7.38-7.95 (4H, m), 8.38 (1H, dd, J = 8Hz, 5Hz), 8.8-9.1 (2H, m), 9.21 (1H, d, J = 2Hz)

Mass (M/Z) : 307 (M^+)

Example 197

To a solution of 2-(4-benzyloxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.18 g) in methanol (12 ml) and tetrahydrofuran (6 ml) was added 10% palladium on carbon (wet ca. 50%, 0.30 g), and the mixture was stirred for 7 hours at ambient temperature under atmospheric pressure of hydrogen gas. The mixture was filtered, and the filtrate was evaporated. The residue was dissolved in methanol (20 ml), and hydrogenated again on palladium on carbon (wet, 0.50 g) for 5 hours. After the filtration, the filtrate was evaporated, and the residue was triturated in a mixture of diisopropyl ether and isopropanol (1:1 V/V) to give 2-(4-hydroxy-2-methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.25 g).

mp : 237-240°C

IR (Nujol) : 1610 cm^{-1}

NMR (DMSO-d_6, δ) : 2.47 (3H, s), 3.89 (3H, s), 6.53 (1H, dd, J = 8Hz, J = 2Hz), 6.60 (1H, d, J = 2Hz), 7.46 (1H, dd, J = 8Hz, J = 5Hz), 7.89 (1H, d, J = 8Hz), 8.07 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.51 (1H, dd, J = 5Hz, J = 2Hz), 8.92 (1H, d, J = 2Hz), 10.0 (1H, br s)

Mass (M/Z) : 281 (M^+)

Example 198

To a solution of 2-(2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (1.0 g) in acetic acid (10 ml) were added a solution of hydrogen bromide in acetic acid (28%, 0.2 ml) and pyridinium hydrobromide perbromide (1.49 g), and was stirred at ambient temperature for 19 hours. Then the mixture was poured into ice-water (100 ml), adjusted to pH 4.8 with 8N sodium hydroxide, and extracted with chloroform. Th organic layer was washed by aqueous sodium bicarbonate and evaporated, and the residue was triturated in diisopropyl ether to give 2-(5-bromo-2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.92 g).

mp : 246-248°C

IR (Nujol) : 1600, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 2.52 (3H, s), 2.96 (3H, s), 3.96 (3H, s), 4.03 (3H, s), 6.89 (1H, s), 7.43 (1H, dd, J = 8Hz, J = 5Hz), 8.11 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.24 (1H, s), 8.47 (1H, dd, J = 2Hz, J = 5Hz), 8.97 (1H, d, J = 2Hz), 11.6 (1H, br s)

Mass (M/Z) : 373 (M^+)

Example 199

To a solution of 2-(2,4-dimethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole (0.9 g) in ethanol (20 ml) was added conc. hydrochloric acid (0.6 ml), and the mixture was evaporated. The resulting syrup was triturated in ethanol to give 2-(2,4-dimethoxyph nyl)-4-methyl-5-(3-pyridyl)imidazol dihydrochloride (1.02 g).

mp : 247-248°C

IR (Nujol) : 1615, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 2.56 (3H, s), 3.91 (3H, s), 4.01 (3H, s), 6.78 (1H, dd, J = 7Hz, J = 2Hz). 6.86 (1H, d, J = 2Hz), 8.3-7.8 (2H, m), 8.87 (1H, ddd, J = 8Hz, J = 2Hz, J = 2Hz), 8.87 (1H, dd, J = 5Hz, J = 2Hz), 9.20 (1H, d, J = 2Hz)

Example 200

2-(2-Methoxy-4-methylsulfinylphenyl)-4-methyl-5-(3-pyridyl) imidazole dihydrochloride was obtained according to a similar manner to that of Example 199.

mp : 212-215°C

IR (Nujol) : 1640, 1600, 1580 cm^{-1}

NMR (DMSO-d_6, δ), : 2.55 (3H, s), 2.84 (3H, s), 4.03 (3H, s), 7.41 (1H, dd, J = 8Hz, J = 2Hz), 7.49 (1H, d, J = 2Hz), 7/.66 (1H, dd, J = 5Hz, J = 8Hz), 8.19 (1H, d, J = 8Hz), 8.28 (1H, ddd, J = 2Hz, J = 2Hz, J = 8Hz), 8.62 (1H, dd, J = 2Hz, J = 5Hz), 8.91 (1H, d, J = 2Hz)

Mass (M/Z) = 327 (M^+, Free)

Example 201

2-[4-(dimethylamino)-2-methoxyphenyl]-4-methyl-5-(3-pyridyl) imidazole was obtained according to a similar manner to that of Example 124.

And then its dihydrochloride was obtained according to a similar manner to that of Example 199.

The following physical data are those of the dihydrochloride.

mp : 218-220°C

IR (Nujol) : 1612, 1519, 1495 cm^{-1}

NMR (D_2O, δ) : 2.58 (3H, s), 3.22 (6H, s), 4.10 (3H, s), 6.83-7.09 (2H, m), 7.85 (1H, d, J = 9Hz), 8.37 (1H, dd, J = 8Hz, 5Hz), 8.70-8.98 (2H, m), 9.10 (1H, s)

Example 202

2-(2-Aminophenyl)-1,5-dimethyl-4-(3-pyridyl)imidazole dihydrochloride was obtained according to a similar manner to that of Example 199.

mp : 285-286°C

IR (Nujol) : 1587, 1512 cm^{-1}

Example 203

To a solution 1-hydroxyimino-1-(3-pyridyl)acetone (0.5 g) in acetic acid (10 ml) was added 2-fluorobenzaldehyde (0.76 g) and ammonium acetate (2.35 g), and refluxed for 30 minutes. Then, the solution was poured into water ~~(75 ml)~~, neutrallized with aqueous potassium carbonate, and extracted with ethyl acetate. The extract was dried over magnesium sulfate and concentrated, and the residue was triturated with diisopropyl ether to give 2-(2-fluorophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole (0.23 g). mp : 65-75°C

IR (Nujol) : 1640, 1572, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 2.25 (3H, s), 7.12-7.80 (5H, m), 7.99 (1H, dd, J = 8Hz, 2Hz, 2Hz), 8.40-8.92 (2H, m)

MASS (M/Z) : 269 (M^+)

Example 204

The following compounds were obtained according to a similar manner to that of Example 1,2,3,4,5 or 203.

(1) 1-Hydroxy-2-(4-methoxycarbonylphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 105-113°C
IR (Nujol) : 1723, 1611 cm^{-1}
NMR (DMSO-d_6, δ) : 2.25 (3H, s), 3.90 (3H, s), 7.46 (1H, dd, J=8Hz, 5Hz), 7.86-8.34 (5H, m), 8.58 (1H, dd, J=5Hz, 2Hz), 8.78 (1H, d, J=2Hz)

(2) 1-Hydroxy-2-(2-mesylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 158-163°C
IR (Nujol) : 1583, 1495 cm^{-1}
NMR (DMSO-d_6, δ) : 2.46 (3H, s), 2.97 (3H, s), 7.20-7.95 (5H, m), 8.20 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.60 (1H, dd, J=5Hz, 2Hz), 8.91 (1H, d, J=2Hz)

(3) 2-(4-Carboxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole mp : 188-192°C
IR (Nujol) : 1708, 1609 cm^{-1}
NMR (D_2O-DCl, δ) : 2.60 (3H, s), 8.15-8.26 (4H, m), 8.39 (1H, dd, J=8Hz, 5Hz), 8.95-9.20 (2H, m), 9.29 (1H, s),
MASS (M/Z) : 295 (M^+)

(4) 1-Hydroxy-2-(2-hydroxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 201-202°C
IR (Nujol) : 1629, 1592, 1572, 1486 cm^{-1}
NMR (DMSO-d_6, δ) : 2.42 (3H, s), 6.80-7.81 (5H, m), 8.19 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.62 (1H, dd, J=5Hz, 2Hz), 8.90 (1H, d, J=2Hz)

(5) 1-Hydroxy-4-methyl-5-(3-pyridyl)-2-(2-trifluoromethylphenyl)imidazole mp : 100-106°C
IR (Nujol) : 1608, 1560, 1482 cm^{-1}
NMR (DMSO-d_6, δ) : 2.32 (3H, s), 7.35-8.13 (6H, m), 8.58 (1H, dd, J=5Hz, 2Hz), 8.80 (1H, d, J=2Hz)

(6) 1-Hydroxy-5-methyl-2-(2-methylthiophenyl)-4-(3-pyridyl)imidazole mp : 80-90°C
IR (Nujol) : 1590, 1550, 1540 cm^{-1}
NMR (DMSO-d_6, δ) : 2.42 (3H, s), 2.48 (3H, s), 7.20-7.70 (5H, m), 8.15 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.49 (1H, d, J=5Hz), 8.96 (1H, d, J=2Hz)
MASS (M/Z) : 297 (M^+)

(7) 1-Hydroxy-4-methyl-5-(3-pyridyl)-2-(4-trifluoromethylphenyl)imidazole NMR (DMSO-d_6, δ) : 2.28 (3H, s), 7.50 (1H, dd, J=8Hz, 5Hz), 7.70-8.40 (5H, m), 8.56 (1H, m), 8.80 (1H, s)

(8) 2-(4-Acetamidophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole mp : 156-161°C
IR (Nujol) : 1690, 1672, 1600, 1530, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.09 (3H, s), 2.21 (3H, s), 7.45 (1H, dd, J=8Hz, 5Hz), 7.50-8.20 (5H, m), 8.52 (1H, dd, J=5Hz, 2Hz), 8.75 (1H, d, J=2Hz), 10.16 (1H, s)

(9) 1-Hydroxy-4-methyl-2-(4-nitrophenyl)-5-(3-pyridyl)imidazole mp : 113-121°C
IR (Nujol) : 1600, 1510 cm^{-1}
NMR (DMSO-d_6, δ) : 2.38 (3H, s), 7.65 (1H, dd, J=8Hz, 5Hz), 8.00-8.55 (5H, m), 8.70 (1H, dd, J=5Hz, 2Hz), 8.85 (1H, d, J=2Hz)

(10) 2-[2-(4-Chlorobenzyloxy)phenyl]-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole mp : 201-203°C
IR (Nujol) : 1620, 1600 cm^{-1}
NMR (DMSO-d_6, δ) : 2.27 (3H, s), 5.20 (2H, s), 6.86-7.77 (9H, m), 7.93 (1H, d t, J=2, 8Hz), 8.55 (1H, dd, J=2, 5Hz), 8.75 (1H, d, J=2Hz)

(11) 1-Hydroxy-4-methyl-2-(2-methyl-4-acetamidophenyl)-5-(3-pyridyl)imidazole mp : 200-204°C (dec.)
IR (Nujol) : 1670, 1610, 1590, 1530 cm^{-1}

(12) 2-(3-Chloro-4-acetamidophenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole mp : 157-159°C (dec.)
IR (Nujol) : 3250, 1700, 1625, 1565, 1505 cm^{-1}
NMR (DMSO-d_6, δ) : 2.17 (3H, s), 2.22 (3H, s), 7.47 (1H, dd, J=5, 8Hz), 7.73-8.17 (3H, m), 8.18 (1H, d, J=2Hz), 8.55 (1H, dd, J=2, 5Hz), 8.75 (1H, d, J=2Hz), 9.57 (1H, s)
MASS (m/e) : 342 (M^+)

(13) 1-Hydroxy-2-(2-methoxy-4-acetamido-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 182-183°C
IR (Nujol) : 3470, 3340, 1695, 1620, 1595, 1500 cm^{-1}
NMR (D_2O + DCl, δ) : 2.43 (3H, s), 2.63 (3H, s), 4.12 (3H, s), 8.17 (1H, s), 8.48 (1H, dd, J=5, 8Hz), 8.83-9.27 (2H, m), 9.05 (1H, s), 9.32 (1H, d, J=2Hz)

(14) 1-Hydroxy-2-(2-methoxy-4-chloro-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 171-172°C (dec.)
IR (Nujol) : 1620, 1600, 1565, 1530, 1520 cm^{-1}
NMR (D_2O + DCl, δ) : 2.67 (3H, s), 4.20 (3H, s), 7.67 (1H, s), 8.45 (1H, dd, J=5, 8Hz), 8.87 (1H, s), 8.90-9.23 (2H, m), 9.32 (1H, d, J=2Hz)

(15) 2-(2-Ethoxyphenyl)-1-hydroxy-4-methyl-5-(3-pyridyl)imidazole mp : 101-103°C
IR (Nujol) : 3350, 1620, 1585, 1250 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, 6) : 1.37 (3H, t, J=7Hz), 2.24 (3H, s), 4.06 (2H, q, J=7Hz), 6.8-7.1 (2H, m), 7.2-7.5 (2H, m), 8.01 (1H, dd, J=2Hz, 7Hz), 8.17 (1H, dd, J=2Hz, 7Hz), 8.48 (1H, dd, J=2Hz, 5Hz), 8.61 (1H, d, J=2Hz)

(16) 1-Hydroxy-2-(2-isopropoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 158-160°C
IR (Nujol) : 3400, 1600, 1570 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 1.41 (6H, d, J=6Hz), 4.72 (1H, septet, J=6Hz), 7.0-7.6 (4H, m), 8.1-8.3 (1H, m), 8.5-8.8 (3H, m)

(17) 1-Hydroxy-4-methyl-2-[2-(2-propynyloxy)phenyl]-5-(3-pyridyl)imidazole mp : 148-150°C
IR (Nujol) : 1600, 1580 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 2.25 (3H, s), 2.62 (1H, t, J=2Hz), 4.76 (2H, d, J=2Hz), 6.8-7.6 (4H, m), 7.8-8.8 (4H, m)

(18) 2-(2-Fluorophenyl)-1-hydroxy-4-methyl-5-(2-pyridyl)imidazole mp : 244-249°C (dec.)
IR (Nujol) : 1590, 1580 cm^{-1}
NMR ($CDCl_3$-CD_3OD, δ) : 2.55 (3H, s), 6.9-7.5 (4H, m), 7.6-7.8 (2H, m), 7.8-8.2 (1H, m), 8.5-8.7 (1H, m)

(19) 2-(2-Fluorophenyl)-1-hydroxy-4-methyl-5-(4-pyridyl)imidazole mp : 249-251°C
IR (Nujol) : 1600, 1210 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 7.2-7.7 (4H, m), 7.82 (2H, dd, J=2Hz, 5Hz), 8.52 (2H, dd, J=2Hz, 5Hz)

(20) 2-(2-Methoxy-4-chloro-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 234-6°C (dec.)
IR (Nujol) : 1600, 1570, 1510 cm^{-1}

(21) 2-[2-(4-Chlorobenzyloxy)phenyl]-4-methyl-5-(3-pyridyl)imidazole mp : 106-108°C
IR (Nujol) : 3410, 1600, 1585, 1550, 1530 cm^{-1}

(22) 4-Methyl-2-(2-methyl-4-acetamidophenyl)-5-(3-pyridyl)imidazole mp : 285-287°C
IR (Nujol) : 3220, 1675, 1620, 1550, 1500 cm^{-1}

(23) 2-(2-Methoxy-4-acetamido-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 220-221°C
IR (Nujol) : 3360, 3330, 1695, 1620, 1590, 1535 cm^{-1}

(24) 2-(2-Ethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 166-168°C
IR (Nujol) : 3230, 1590, 1555, 1520 cm^{-1}

(25) 2-(2-Isopropoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 168-169°C
IR (Nujol) : 3420, 1590, 1560, 1235 cm^{-1}

(26) 4-Methyl-2-[2-(2-propynyloxy)phenyl]-5-(3-pyridyl)imidazole mp : 167-169°C
IR (Nujol) : 3320, 1590, 1560, 1510 cm^{-1}

(27) 2-(2-Fluorophenyl)-4-methyl-5-(2-pyridyl)imidazole mp : 128-130°C IR (Nujol) : 1600, 1590, 1490 cm^{-1}

(28) 2-(2-Fluorophenyl)-4-methyl-5-(4-pyridyl)imidazole mp : 192-193°C
IR (Nujol) : 1595, 1570 cm^{-1}

(29) 2-(2-Fluorophenyl)-4-(3-pyridyl)imidazole mp : 144-145°C
IR (Nujol) : 1605, 1586, 1556, 1485 cm^{-1}

(30) 2-(2-Hydroxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 265-266°C
IR (Nujol) : 1600, 1575, 1494 cm^{-1}

(31) 2-(2-Mesylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 245-246°C
IR (Nujol) : 1600, 1577, 1497 cm^{-1}

(32) 2-(4-Methoxycarbonylphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 160-168°C
IR (Nujol) : 1733, 1616, 1600, 1569 cm^{-1}

(33) 2-(4-Carboxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : >280°C
IR (Nujol) : 1675, 1611, 1568 cm^{-1}

(34) 4-M thyl-2-(2-m thylthiophenyl)-5-(3-pyridyl)imidazole mp : 200-201°C
IR (Nujol) : 1600, 1576, 1489 cm^{-1}

(35) 4-Methyl-5-(3-pyridyl)-2-(2-trifluorom thylphenyl)imidazole mp : 131-132°C
IR (Nujol) : 1609, 1575, 1500 cm^{-1}

(36) 2-(4-Acetamido-3-chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 262-264°C
IR (Nujol) : 3210, 1665, 1580, 1540 cm^{-1}

(37) 2-(2-Methoxy-4-chloro-5-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 173-175°C
IR (Nujol) : 3300, 3200, 1630, 1580, 1565, 1520 cm^{-1}

(38) 2-(2-Methoxy-4-chloro-5-acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 274-276°C (dec.)
IR (Nujol) : 3250, 1660, 1600, 1590, 1570, 1535 cm^{-1}

(39) 1-Hydroxy-4-methyl-5-(3-pyridyl)-2-(2-tosylaminophenyl)imidazole mp : 103-113°C
IR (Nujol) : 3520, 1658, 1590 cm^{-1}
NMR (DMSO-d_6, δ) : 2.32 (6H, s), 7.10-7.78 (9H, m), 8.24 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.65 (1H, dd, J=5Hz, 2Hz), 8.95 (1H, d, J=2Hz)

(40) 4-Methyl-5-(3-pyridyl)-2-(2-tosylaminophenyl)imidazole mp : 282-284°C
IR (Nujol) : 3530, 1665, 1599, 1570, 1495 cm^{-1}

(41) 4-Methyl-2-[2-(3-nitrobenzoylamino)phenyl]-5-(3-pyridyl)imidazole mp: 257-259°C
IR (Nujol) : 1675, 1625, 1600, 1525, 1490 cm^{-1}

(42) 4-Methyl-2-[2-(3-methylthioureido)phenyl]-5-(3-pyridyl)imidazole mp: 192-193°C
IR (Nujol) : 1570, 1520, 1490 cm^{-1}

(43) 2-[2-(3-benzoylthioureido)phenyl]-4-methyl-5-(3-pyridyl)imidazole mp: 159-161°C
IR (Nujol) : 3405, 3180, 2070, 1680, 1615, 1582, 1510 cm^{-1}

(44) 2-(2-methoxycarbonylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp: 221-223°C
IR (Nujol) : 1732, 1599, 1570, 1538, 1490 cm^{-1}

Example 205

A mixture of 1-hydroxy-2-(2-methoxy-4-chloro-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole (9.7 g) and triethyl phosphite (8.9 g) in N,N-dimethylformamide (100 ml) was stirred at 80-90°C for one hour. The reaction mixture was poured into water and the resultant mixture was stirred at ambient temperature for one hour. The precipitate was collected by filtration and washed with water and ethyl acetate and dried to give 2-(2-methoxy-4-chloro-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole (7.6 g). mp : 234-236°C (dec.)
IR (Nujol) : 1600, 1570, 1510 cm^{-1}
NMR (D_2O + DCl, δ) : 2.68 (3H, s), 4.22 (3H, s), 7.63 (1H, s), 8.38 (1H, dd, J=5, 8Hz), 8.78 (1H, s), 8.92-9.17 (2H, m), 9.28 (1H, d, J=2Hz)
MASS (m/e) : 344 (M^+)

Example 206

The following compounds were obtained according to a similar manner to that of Example 120, 121, 122, 123, 124 or 205.

(1) 2-[2-(4-Chlorobenzyloxy)phenyl]-4-methyl-5-(3-pyridyl)imidazole mp : 106-108°C (recrystallized from a mixture of ethyl acetate and diethyl ether)
IR (Nujol) : 3410, 1600, 1585, 1550, 1530 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 5.36 (2H, s), 6.85-7.63 (9H, m), 8.03 (1H, dd, J=2, 8Hz), 8.40 (1H, dd, J=2, 5Hz), 8.90 (1H, d, J=2Hz), 11.70 (1H, br s)
MASS (m/e) : 375 (M^+)

(2) 4-Methyl-2-(2-methyl-4-acetamidophenyl)-5-(3-pyridyl)imidazole mp : 285-287°C (recrystallized from a mixture of methanol and ethyl acetate)
IR (Nujol) : 3220, 1675, 1620, 1550, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.06 (3H, s), 2.47 (3H, s), 2.60 (3H, s), 7.36 (1H, dd, J=5, 8Hz), 7.43-7.60 (3H, m), 8.00 (1H, d t, J=2, 8Hz), 8.37 (1H, dd, J=2, 5Hz), 8.86 (1H, d, J=2Hz), 9.66 (1H, s), 12.10 (1H, br s)
MASS (m/e) : 306 (M^+)

(3) 2-(2-Methoxy-4-acetamido-5-nitrophenyl)-4-methyl-5(3-pyridyl)imidazole mp : 220-221°C
IR (Nujol) : 3360, 3330, 1695, 1620, 1590, 1535 cm^{-1}
NMR (DMSO-d_6, δ) : 2.20 (3H, s), 2.53 (3H, s), 4.11 (3H, s), 7.47 (1H, dd, J=5, 8Hz), 7.90 (1H, s), 8.12 (1H, d t, J=2, 8Hz), 8.48 (1H, dd, J=2, 5Hz), 8.77 (1H, s), 8.95 (1H, d, J=2Hz), 10.42 (1H, br s), 11.70 (1H, m)

(4) 2-(2-Ethoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 166-168°C
IR (Nujol) : 3230, 1590, 1555, 1520 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 1.56 (3H, t, J=7Hz), 2.47 (3H, s), 4.24 (2H, q, J=7Hz), 6.9-7.6 (4H, m), 7.9-8.5 (3H, m), 8.85 (1H, d, J=2Hz)
MASS (m/e) : 279 (M^+)

(5) 2-(2-Isopropoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 168-169°C
IR (Nujol) : 3420, 1590, 1560, 1235 cm^{-1}
NMR (CD_3OD + $CDCl_3$, δ) : 1.35 (6H, d, J=6.5Hz), 2.53 (3H, s), 4.80 (1H, sep, J=6.5Hz), 6.9-7.6 (4H, m), 7.9-8.5 (3H, m), 8.84 (1H, d, J=3Hz)
MASS (m/e) : 293 (M^+)

(6) 4-Methyl-2-[2-(2-propynyloxy)phenyl]-5-(3-pyridyl)imidazole mp : 167-169°C
IR (Nujol) : 3320, 1590, 1560, 1510 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 2.51 (3H, s), 2.77 (1H, t, J=2Hz), 4.86 (2H, d, J=2Hz), 6.9-7.5 (4H, m), 7.9-8.5 (3H, m), 8.83 (1H, d, J=2Hz)
MASS (m/e) : 289 (M^+)

(7) 2-(2-Fluorophenyl)-4-methyl-5-(2-pyridyl)imidazole mp : 128-130°C
IR (Nujol) : 1600, 1590, 1490 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 2.61 (3H, s), 5.40 (1H, br s), 6.9-7.4 (4H, m), 7.6-7.8 (2H, m), 8.0-8.4 (1H, m), 8.4-8.6 (1H, m)
MASS (m/e) : 253 (M^+)

(8) 2-(2-Fluorophenyl)-4-methyl-5-(4-pyridyl)imidazole mp : 192-193°C
IR (Nujol) : 1595, 1570 cm^{-1}
NMR ($CDCl_3$ + CD_3OD, δ) : 2.52 (3H, s), 6.9-7.4 (3H, m), 7.65 (2H, dd, J=2Hz, 5Hz), 8.53 (2H, dd, J=2Hz, 5Hz), 8.0-8.4 (1H, m)
MASS (m/e) : 253 (M^+)

(9) 2-(2-Fluorophenyl)-4-(3-pyridyl)imidazole mp : 144-145°C
IR (Nujol) : 1605, 1586, 1556, 1485 cm^{-1}
NMR (DMSO-d_6, δ) : 7.25-7.68 (4H, m), 8.00-8.20 (2H, m), 8.28 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.48 (1H, dd, J=5Hz, 2Hz), 9.22 (1H, d, J=2Hz)
MASS (M/Z) : 239 (M^+)

(10) 2-(2-Hydroxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 265-266°C
IR (Nujol) : 1600, 1575, 1494 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 6.75-7.03 (2H, m), 7.20 (1H, dd, J=8Hz, 2Hz), 7.44 (1H, dd, J=8Hz, 5Hz), 7.70-8.11 (2H, m), 8.46 (1H, dd, J=5Hz, 2Hz), 8.85 (1H, d, J=2Hz)
MASS (M/Z) : 251 (M^+)

(11) 2-(2-Mesylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 245-246°C
IR (Nujol) : 1600, 1577, 1497 cm^{-1}
NMR (DMSO-d_6, δ) : 2.54 (3H, s), 3.11 (3H, s), 7.08-7.68 (4H, m), 7.81-8.11 (2H, m), 8.47 (1H, dd, J=3Hz, 2Hz), 8.93 (1H, d, J=2Hz), 12.83 (1H, br s)

(12) 2-(4-Methoxycarbonylphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 160-168°C
IR (Nujol) : 1733, 1616, 1600, 1569 cm^{-1}
NMR (DMSO-d_6, δ) : 2.56 (3H, s), 3.90 (3H, s), 7.42 (1H, dd, J=8Hz, 5Hz), 7.88-8.30 (5H, m), 8.43 (1H, dd, J=5Hz, 2Hz), 8.92 (1H, d, J=2Hz)
MASS (M/Z) : 293 (M^+)

(13) 2-(4-Carboxyphenyl)-4-methyl-5-(3-pyridyl)imidazole mp : >280°C
IR (Nujol) : 1675, 1611, 1568 cm^{-1}
NMR (DMSO-d_6, δ) : 2.69 (3H, s), 7.61 (1H, dd, J=8Hz, 5Hz), 8.05-8.40 (5H, m), 8.61 (1H, d, J=5Hz), 9.09 (1H, s)
MASS (M/Z) : 279 (M^+)

(14) 4-Methyl-2-(2-methylthiophenyl)-5-(3-pyridyl)imidazole mp : 200-201°C
IR (Nujol) : 1600, 1576, 1489 cm^{-1}
NMR (DMSO-d_6, δ) : 2.40 (3H, s), 2.50 (3H, s), 7.12-7.76 (5H, m), 8.09 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.42 (1H, dd, J=5Hz, 2Hz), 8.96 (1H, d, J=2Hz)
MASS (M/Z) : 281 (M^+)

(15) 4-Methyl-5-(3-pyridyl)-2-(2-trifluoromethylphenyl)imidazole mp : 131-132°C
IR (Nujol) : 1609, 1575, 1500 cm^{-1}
NMR (DMSO-d_6, δ) : 2.52 (3H, s), 7.45 (1H, dd, J=8Hz, 5Hz), 7.60-8.00 (4H, m), 8.10 (1H, ddd, J=8Hz, 2Hz, 2Hz), 8.45 (1H, dd, J=5Hz, 2Hz), 8.95 (1H, d, J=2Hz)
MASS (M/Z) : 303 (M^+)

(16) 2-(4-Acetamido-3-chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 262-264°C
IR (Nujol) : 3210, 1665, 1580, 1540 cm^{-1}
NMR (DMSO-d_6, δ) : 2.16 (3H, s), 2.52 (3H, s), 7.40 (1H, dd, J=5, 8Hz), 7.87 (2H, s), 8.84 (2H, br s), 8.43 (1H, d, J=5Hz), 8.91 (1H, br s), 9.50 (1H, s), 12.53 (1H, br s)

(17) 4-Methyl-5-(3-pyridyl)-2-(2-tosylaminophenyl)imidazole mp : 282-284°C
IR (Nujol) : 3530, 1665, 1599, 1570, 1495 cm^{-1}
NMR (DMSO-d_6, δ) : 2.24 (3H, s), 2.50 (3H, s), 6.95-7.91 (9H, m), 8.04 (1H, d, J=8Hz), 8.48 (1H, d, J=5Hz), 8.95 (1H, s), 13.00 (1H, br s)

(18) 2-(2-Methoxy-4-chloro-5-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 173-175°C
IR (Nujol) : 3300, 3200, 1630, 1580, 1565, 1520 cm^{-1}

(19) 2-(2-Methoxy-4-chloro-5-acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 274-276°C (dec.)
IR (Nujol) : 3250, 1660, 1600, 1590, 1570, 1535 cm^{-1}

(20) 4-Methyl-2-[2-(3-nitrobenzoylamino)phenyl]-5-(3-pyridyl)imidazole mp: 257-259°C
IR (Nujol) : 1675, 1625, 1600, 1525, 1490 cm^{-1}

(21) 4-Methyl-2-[2-(3-methylthioureido)phenyl]-5-(3-pyridyl)imidazole mp: 192-193°C
IR (Nujol) : 1570, 1520, 1490 cm^{-1}

(22) 2-[2-(3-benzoylthioureido)phenyl]-4-methyl-5-(3-pyridyl)imidazole mp: 159-161°C
IR (Nujol) : 3405, 3180, 2070, 1680, 1615, 1582, 1510 cm^{-1}

(23) 2-(2-methoxycarbonylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole mp: 221-223°C
IR (Nujol) : 1732, 1599, 1570, 1538, 1490 cm^{-1}

Example 207

A mixture of 2-(2-methoxy-4-chloro-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole (6.4 g), 1N-hydrochloric acid (37 ml) and 10% palladium on carbon (3 g) in methanol (100 ml) was subjected to catalytic reduction at ambient temperature under atomspheric pressure of hydrogen gas for 3 hours. The reaction mixture was filtered and the filtrate was evaporated in vacuo. The residue was dissolved in water and the solution was adjusted to pH 8.0 with 20% aqueous potassium carbonate. The resultant mixture was extracted with ethyl acetate and extract was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was subjected to column chromatography on silica gel and eluted with a mixture of chloroform and methanol (96:4 V/V). The fractions containing object compound were evaporated in vacuo and the residue was recrystallized from a mixture of ethyl acetate and diisopropyl ether to give 2-(2-methoxy-4-chloro-5-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (2.1 g).

mp : 173-175°C
IR (Nujol) : 3300, 3200, 1630, 1580, 1565, 1520 cm^{-1}
NMR (DMSO-d_6, δ), : 2.55 (3H, s), 3.90 (3H, s) 5.03 (2H, s), 7.09 (1H, s), 7.45 (1H, dd, J=5, 8Hz), 7.70 (1H, s), 8.08 (1H, dt, J=2, 8Hz), 8.45 (1H, dd, J=2, 5Hz), 8.97 (1H, d, J=2Hz), 11.50 (1H, br s)
MASS (m/e) : 314 (M^+)

Example 208

A solution of 2-(2-methoxy-4-chloro-5-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (1.0 g) and acetic anhydride (2 ml) in a mixture of ethyl acetate (20 ml) and tetrahydrofuran (10 ml) was refluxed for 2 hours. The reaction mixture was cooled with ice-water and the crystalline residue was collected by filtration to give 2-(2-methoxy-4-chloro-5-acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.7 g).

mp : 274-276°C (dec.)

IR (Nujol) : 3250, 1660, 1600, 1590, 1570, 1535 cm^{-1}

NMR (D_2O + DCl, δ) : 2.30 (3H, s), 2.65 (3H, s), 4.06 (3H, s), 7.45 (1H, s), 8.06 (1H, s), 5.70 (1H, dd, J=5, 7Hz), 8.83-9.06 (2H, m), 9.21 (1H, d, J=2Hz)

MASS (m/e) : 356 (M^+)

Example 209

The following compounds were obtained according to a similar manner to that of Example 195 or 208.

(1) 2-(4-Acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole mp : 239-240°C
IR (Nujol) : 3400, 1680, 1590, 1520, 1490 cm^{-1}

(2) 2-(4-Acetamido-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole mp : 215-218°C
IR (Nujol) : 1675, 1600 cm^{-1}

(3) 4-Methyl-2-(2-methyl-4-acetamidophenyl)-5-(3-pyridyl)imidazole mp : 285-287°C
IR (Nujol) : 3220, 1675, 1620, 1550, 1500 cm^{-1}

(4) 2-(2-Methoxy-4-acetamido-5-nitrophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 220-221°C
IR (Nujol) : 3360, 3330, 1695, 1620, 1590, 1535 cm^{-1}

(5) 2-(4-Acetamido-3-chlorophenyl)-4-methyl-5-(3-pyridyl)imidazole mp : 262-264°C
IR (Nujol) : 3210, 1665, 1580, 1540 cm^{-1}

Example 210

2-(2-Methoxyphenyl)-4-methyl-5-(3-pyridyl)imidazole dihydrochloride was obtained according to a similar manner to that of Example 199.

mp : 228-230°C

IR (Nujol) : 1630, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 2.60 (3H, s), 4.01 (3H, s), 8.4-7.0 (5H, m), 9.0-8.6 (2H, m), 9.24 (1H, d, J=2Hz)

Example 211

To a solution of 2-(2-Aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.8 g) and triethylamine (0.49 ml) in methylene chloride (10 ml) was added a solution of 3-nitrobenzoyl chloride (0.65 g) in methylene chloride (5 ml) under ice cooling. The reaction solution was stirred for one hour. The reaction mixture was poured into water (50 ml), extracted with a mixture of chloroform and methanol, and dried over magnesium sulfate. The solvent was distilled off, and a residu was triturated with ethyl acetate to give 4-methyl-2-[2-(3-nitrobenzoylamino)phenyl]-5-(3-pyridyl)imidazole (0.95 g).

mp : 257-259°C
IR (Nujol) : 1675, 1625, 1600, 1525, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.51 (3H, s), 7.10-8.20 (6H, m), 8.31-8.95 (6H, m)

Example 212

To a solution of 2-(2-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.8 g) in tetrahydrofuran (10 ml) was added methyl isothiocyanate (0.33 ml) at ambient temperature. The reaction mixture was stirred at ambient temperature for one hour, and refluxed for 20 hours. The resulting precipiate was collected by filtration, and washed with tetrahydrofuran and diethyl ether to give 4-methyl-2-[2-(3-methylthioureido)phenyl]-5-(3-pyridyl)imidazole (0.71 g).
mp : 192-193°C
IR (Nujol) : 1570, 1520, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 2.95 (3H, d, J = 5Hz), 6.98-7.52 (3H, m), 7.68-8.60 (5H, m), 8.99 (1H, s), 14.30 (1H, s), 15.07 (1H, s)

Example 213

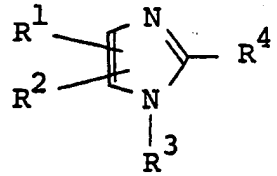
To a solution of 2-(2-aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (1.60 g) in methylene chloride (20 ml) was added a solution of benzoyl isothiocyanate (1.04 g) in methylene chloride (5 ml) at ambient temperature. The reaction mixture was stirred at ambient temperature for one hour. The resulting precipitate was collected by filtration. The precipitate was washed with methylene chloride, ethanol, and diethyl ether to give 2-[2-(3-benzoylthioureiedo)phenyl]-4-methyl-5-(3-pyridyl)imidazole (1.95 g).
mp : 159-161°C
IR (Nujol) : 3405, 3180, 2070, 1680, 1615, 1582, 1510 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 7.00-8.49 (12H, m), 8.97 (1H, s), 11.38 (1H, s)

Example 214

To a suspension of 2-(2-Aminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.80 g) and triethylamine (0.49 ml) in methylene chloride (10 ml) was added methyl chloroformate (0.27 ml) under ice-cooling.
The reaction mixture was stirred at ambient temperature for one hour and the resulting precipitate was collected by filtration and triturated by water and ethyl acetate. The residue was recrystallized from ethanol to give 2-(2-methoxycarbonylaminophenyl)-4-methyl-5-(3-pyridyl)imidazole (0.50 g).
mp : 221-223°C
IR (Nujol) : 1732, 1599, 1570, 1538, 1490 cm^{-1}
NMR (DMSO-d_6, δ) : 2.50 (3H, s), 3.73 (3H, s), 7.00-7.55 (3H, m), 7.80-8.11 (2H, m), 8.20-8.54 (2H, m), 8.94 (1H, s)

Claims

1. A compound of the formula:



wherein

R^1 is pyridyl,

R^2 is hydrogen, lower alkyl or hydroxy(lower) alkyl,

R^3 is hydrogen, hydroxy or lower alkyl, and

R^4 is aryl optionally substituted with substituent (s) selected from the group consisting of lower alkylthio lower alkylsulfinyl, lower alkylsulfonyl, nitro, amino substituted amino, hydroxy, lower alkoxy, lower alkynyloxy, substituted or unsubstituted ar(lower)alkoxy, halogen, halo(lower)alkyl, carboxy and esterified carboxy,

and a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein R^4 is phenyl which may be substituted with substituent (s) select d from the group consisting of lower alkyl, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, nitro, amino, mono-or di(lower) alkylamino, lower alkanoylamino, nitro substituted or unsubstituted benzoylamino, lower alkoxycarbonylamino, phenyl(lower) alkoxycarbonylamino, lower alkanesulfonylamino, lower alkyl substituted benzenesulfonylamino, ureido, thioureido, lower alkylureido, lower alkylthioureido, N-lower alkanoyl-N-lower alkylamino, hydroxy, benzoylthioureido, lower alkoxy, lower alkynyloxy, halogen substituted or unsubstituted phenyl(lower)alkoxy, halogen, halo(lower)alkyl, carboxy and lower alkoxycarbonyl.

3. A compound of claim 2, wherein R^2 is lower alkyl, R^3 is hydrogen, and R^4 is phenyl substituted with substituent(s) selected from the group consisting of lower alkylthio, lower alkanoylamino, lower alkoxy and halogen.

4. A compound of claim 3, wherein R^4 is phenyl substituted with lower alkoxy.

5. A compound of claim 4, which is 2-(2-methoxyphenyl)-5-methyl-4-(3-pyridyl)imidazole.

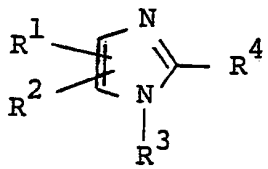
6. A compound of claim 3, wherein R^4 is phenyl substituted with lower alkanoylamino.

7. A compound of claim 6, which is 2-(2-acetamidophenyl)-4-methyl-5-(3-pyridyl)imidazole.

8. A compound of claim 3, wherein R^4 is phenyl substituted with lower alkanoylamino, lower alkoxy and halogen.

9. A compound of claim 8, which is 2-(4-acetamido-5-chloro-2-methoxyphenyl)-5-methyl-4-(3-pyridyl)-imidazole.

10. A process for preparing a compound of the formula :



wherein

R^1 is pyridyl,

R^2 is hydrogen, lower alkyl or hydroxy(lower)alkyl,

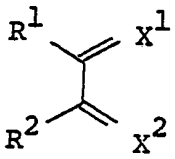
R^3 is hydrogen, hydroxy or lower alkyl, and

R4 is aryl optionally substituted with substituent(s) selected from the group consisting of lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, nitro, amino, substituted amino, hydroxy, lower alkoxy, lower alkynyloxy,substituted or unsubstituted ar(lower)alkoxy, halogen, halo(lower)alkyl, carboxy and esterified carboxy,

or a salt thereof,

which comprises

a) reacting a compound of the formula :

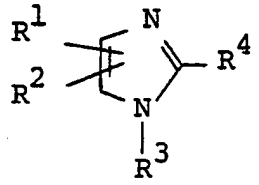


wherein one of X^1 and X^2 is O and the other is a group of the formula : $=N-R^3$, in which R^3 is as defined above, and R^1 and R^2 are each as defined above,

or its salt with a compound of the formula :

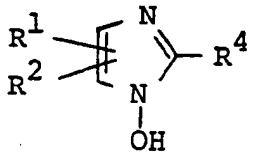
R^4-CHO

wherein R^4 is as d fined above,
or its salt in the presence of ammonia or an agent which liberates ammonia to give a compound of the formula :

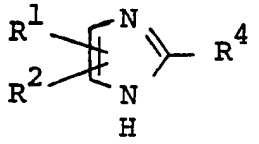


wherein R^1, R^2, R^3 and R^4 are each as defined above,
or its salt, or

b) reducing a compound of the formula :

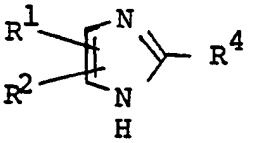


wherein R^1, R^2 and R^4 are each as defined above,
or its salt to give a compound of the formula :

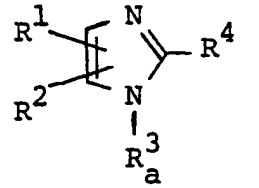


wherein R^1, R^2 and R^4 are each as defined above,
or its salt, or

c) subjecting a compound of the formula :



wherein R^1, R^2 and R^4 are each as defined above,
or its salt to lower alkylation reaction to give a compound of the formula :



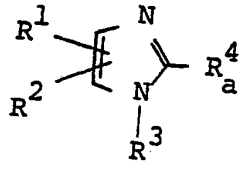
wherein

R^3_a is lower alkyl, and

R^1, R^2 and R^4 are each as defined above,

or its salt, or

d) subjecting a compound of the formula :

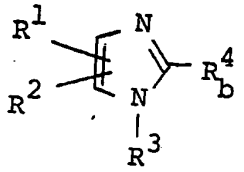


wherein

R^4_a is aryl substituted with acylamino and lower alkoxy, with acylamino, lower alkoxy and halogen, or with N-acyl-N-lower alkylamino, lower alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined above,

or its salt to elimination reaction of the acyl group to give a compound of the formula :



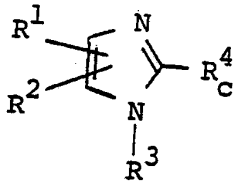
wherein

R^4_b is aryl substituted with amino and lower alkoxy, with amino, lower alkoxy and halogen, or with lower alkylamino, lower alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined above,

or its salt, or

e) reacting a compound of the formula :

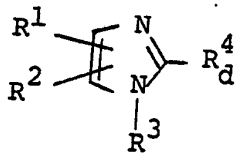


wherein

R^4_c is aryl substituted with amino, with amino and lower alkyl, with amino and lower alkoxy, with amino and halogen, with amino, lower alkoxy and nitro, or with amino, lower alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined above,

or its salt with an acylating agent to give a compound of the formula :



wherein

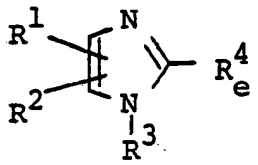
R^4_d is aryl substituted with acylamino, with acylamino and lower alkyl, with acylamino and lower

alkoxy, with acylamino and halogen, with acylamino, lower alkoxy and nitro, or with acylamino, lower alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined abov

or its salt, or

f) oxidizing a compound of the formula :

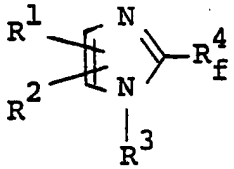


wherein

R^4_e is aryl substituted with lower alkylthio and lower alkoxy, and

R^1, R^2 and R^3 are each as defined above,

or its salt to give a compound of the formula :



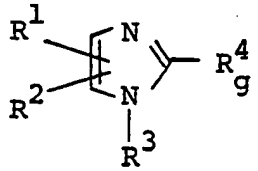
wherein

R^4_f is aryl substituted with lower alkylsulfinyl and lower alkoxy, or with lower alkylsulfonyl and lower alkoxy, and

R^1, R^2 and R^3 are each as defined above,

or its salt, or

g) reducing a compound of the formula :

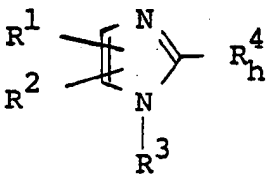


wherein

R^4_g wherein is aryl substituted with nitro, with nitro and lower alkoxy, or with nitro, lower alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined above,

or its salt to give a compound of the formula :



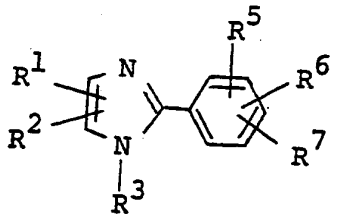
wherein

R^4_h is aryl substituted with amino, with amino and lower alkoxy, or with amino, low r alkoxy and halogen, and

R^1, R^2 and R^3 are each as defined above,

or its salt, or

h) reducing a compound of the formula :



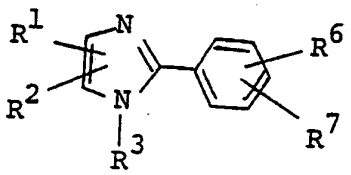
wherein

R^5 is halogen,

R^6 and R^7 are each lower alkoxy or substituted amino, and

R^1, R^2 and R^3 are each as defined above,

or its salt to give a compound of the formula :

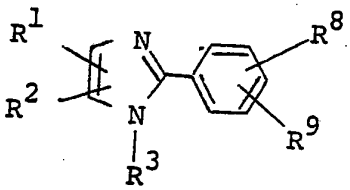


wherein

R^1, R^2, R^3, R^6 and R^7 are each as defined above,

or its salt, or

i) halogenating a compound of the formula :

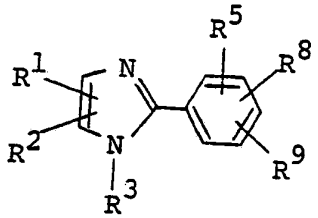


wherein

R^8 and R^9 are each lower alkoxy, and

R^1, R^2 and R^3 are each as defined above,

or its salt to give a compound of the formula :

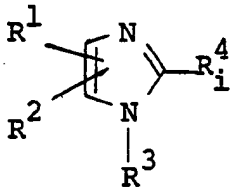


wherein

R^1, R^2, R^3, R^5, R^8 and R^9 are each as defined above,

or its salt or

j) reducing a compound of the formula :

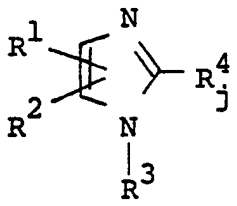


wherein

R^4_i is aryl substituted with ar(lower)alkoxy and lower alkoxy, and

R^1, R^2 and R^3 are each as defined above,

or its salt to give a compound of the formula :



wherein

R^4_j is aryl substituted with hydroxy and lower alkoxy, and

R^1, R^2 and R^3 are each as defined above,

or its salt.

11. A pharmaceutical composition comprising a compound of claim 1, as an active ingredient, in association with a pharmaceutically acceptable, substantially nontoxic carrier or excipient.

European Patent Office

EUROPEAN SEARCH REPORT

Application number

EP 87 30 7051

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
X	DE-A-2 155 558 (PFIZER INC.) * page 2, line 22 - page 3, line 16; page 9, line 14 - page 10, line 11; page 34, lines 28, 31, 32 * & US - A - 3 707 475 (Cat. D)	1-4,10,11	C 07 D 401/04 A 61 K 31/44 // C 07 D 213/53
X	DE-A-2 221 546 (CIBA-GEIGY AG) * page 5, line 17 - page 7, line 10; pages 33, 34 *	10	
A	DE-A-2 608 448 (MERCK & CO. INC.) * page 2, line 11 - page 3, line 19; page 15, line 11 - page 16, line 2; page 26, line 32 - page 27, line 31; example 38 * & US - A - 4 440 774 (Cat. D)	1,10,11	

TECHNICAL FIELDS SEARCHED (Int. Cl.4)
C 07 D 401/00 A 61 K 31/00

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	28-10-1987	VAN AMSTERDAM L.J.P.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

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